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Biotechnology assessment and strategic recommendations

Interlink Biotechnologies, LLC

December, 2008

POLÍTICA DE PUBLICACIONES

El CNIC pone a disposición de la comunidad nacional el informe de InterLink Biotechnologies, documento que servirá como insumo para la reflexión del Consejo y la elaboración de recomendaciones sobre el desarrollo de la actividad científico-tecnológica nacional y que, por tanto, no representa una opinión oficial del Consejo de Innovación.

Presentación

Tras la entrega de su propuesta de Estrategia Nacional de Innovación para la Competitividad, el Consejo de Innovación (CNIC), se ha abocado a la elaboración de orientaciones para el fortalecimiento de la actividad científica y tecnológica nacional que contribuyan al logro de los desafíos de competitividad del país.

Dentro de este marco, el CNIC decidió realizar una revisión estratégica del esfuerzo de investigación que nuestro país está haciendo en biotecnología, plataforma transversal que se identifica mundialmente como de alto impacto para el desarrollo de importantes sectores económicos y, en especial, de varios de los sectores priorizados en la Estrategia Nacional de Innovación.

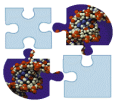
Para desarrollar este estudio el Consejo contrató a InterLink Biotechnologies (EE.UU.), empresa experta en transferencia tecnológica con foco en biotecnología, que cuenta tanto con una base científica de excelencia como con desarrollos industriales. InterLink constituyó un grupo de expertos (cuyos currículos se adjuntan a este informe), de manera tal que la revisión estratégica incluyera el impacto de la biotecnología en sectores como la minería, la agroindustria y la industria forestal, y además en productos y áreas específicas, como alimentos funcionales, nutracéuticos, drogas botánicas y biomedicina. Así, el análisis incluyó bio-industrias como la bio-minería, energía, productos químicos, tratamiento de residuos industriales, entre otros, y la biotecnología agrícola.

El grupo de expertos, en primer lugar, analizó bases públicas de información sobre proyectos biotecnológicos que cuentan con financiamiento público[1], para luego, durante la primera semana de diciembre de 2008, entrevistarse con 21 líderes de los grupos investigación a cargo de los proyectos que el grupo experto identificó como representativos de la información analizada.

Dado que el objetivo del estudio era entregar una opinión experta respecto del impacto potencial en la economía nacional del esfuerzo público en biotecnología, el análisis del grupo experto se limita a identificar factores relevantes para el éxito *económico* de los desarrollos tecnológicos, actuales y potenciales, derivados de los proyectos estudiados. En particular, el análisis utiliza como principal factor de análisis el nivel de "alineamiento" de la investigación biotecnológica nacional con los sectores industriales que podrían beneficiarse de los resultados de tal investigación y redundar así en beneficios económicos. Por tanto, el informe del del grupo experto no evalúa el valor científico de estas investigaciones, ni la excelencia de los grupos que la llevan adelante, si bien InterLink destaca el alto nivel de excelencia científica de los proyectos revisados.

Finalmente, el Consejo expresa su especial agradecimiento a los investigadores y profesionales que se entrevistaron con el grupo de expertos.

[1] - CORFO (2007) "Partnering Opportunities for Applied Research in Biotechnology in Chile".
- IDEA Consultora (2008) "Estudio sobre el potencial de la industria biotecnológica como plataforma para aumentar la competitividad de los sectores productivos con potencial identificados en Chile".



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NATIONAL BIOTECHNOLOGY ASSESSMENT AND STRATEGIC RECOMMENDATIONS

PREPARED FOR

CONSEJO NACIONAL DE INNOVACION PARA LA COMPETITIVIDAD

SANTAGO, CHILE

December 1 – 6, 2008

December 23, 2008

EXECUTIVE SUMMARY

INTRODUCTION AND METHODOLOGY

InterLink Biotechnologies (ILB) consulting group conducted an in depth review of research and development programs in biotechnology related to key sectors of the Chilean industry. The review was conducted from December 1 through the 6, 2008 in Santiago. Prior to travelling to Chile, ILB received written information and spreadsheets containing more than 200 R&D government supported programs from the Consejo Nacional de Innovacion para la Competitividad ("CNIC") for initial review. Together with the information provided by ILB's official Chilean contacts from the CNIC, ILB found a number of previous reviews of the Chilean biotechnology industry, which were helpful in providing additional information. ILB reviewed the background information provided and selected 23 Program Leaders for direct face-to-face interviews to discuss their research strategy and specific research projects under their direction. The total number of research projects evaluated during the face-to-face discussions exceeded 50 and included projects in the areas of agriculture (fruits), nutrition/functional foods, biomass conversion (bio-fuels), bio-mining, biomedicine, diagnostics, nutraceuticals and natural products. The sectors including biomass conversion (industrial waste, new chemicals and products), nutraceuticals, botanical drugs and functional foods were not assessed in detail because limited or no information of specific projects was available in the original listing provided to ILB.

FINDINGS

The ILB team met and interviewed the various biotechnology program leaders in Chile and searched for specific factors separating programs potentially generating high returns on investment from those with lower or low potential returns. It was found that the single greatest influence on return for research expenditure was the degree to which the biotechnological research was aligned to industry sectors in Chile. All the programs reviewed were thus divided into one of three categories: (1) Biotechnology Strongly Aligned to Industry Sectors in Chile, (2) Biotechnology Less Strongly Aligned to Industry Sectors in Chile, and (3) Biotechnology Unaligned to Industry Sectors in Chile that Could Benefit.

Biotechnology programs strongly aligned to industry sectors included (1) the fruit industry and (2) bio-mining. In these biotechnology programs, resource allocation appeared to have a significant, immediate impact in that they addressed important stakeholder problems enabling continuous sector growth and global leadership.

In general, the fruit industry programs are well aligned with the needs and business strategies of the fruit sector (growers, processors and exporters) to enable the continuous growth and world leadership of this sector. Important problems such as the development of new proprietary varieties incorporating important input traits (disease resistance, drought tolerance, adaption to salinity etc) and key quality traits (post harvest and other quality traits) are being addressed applying biotechnology tools in combination with conventional breeding. Programs such as the genetic transformation of grapes and stone fruits and the related genomic programs associated with these species should be considered as technology platforms that are a key requirement for the development of new products in support of the fruit industry.

There is a need to allocate more resources to breeding programs supported by biotechnology tools (genetic markers etc.). The present breeding programs lack the required critical mass to make a significant impact in the industry, perpetuating the

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dependency on foreign varieties that do not always meet the international market needs and local growing conditions. There is, however, duplication of efforts in several areas (grape transformation, genomic initiatives, disease resistance in grapes among others). This duplication of effort may promote unhealthy competition, which in turn becomes an obstacle to reach common objectives.

The bio-mining program has strong applications of basic microbiology and potential applications of biotechnology to mining industry issues. The use of natural microorganisms for the isolation of copper in low-grade ores is very promising and we look forward to the full implementation of the industrial scale process. Further, biotechnological approaches employing microorganisms could be employed to address the following Chilean environmental problems; heavy metal pollution (biotechnology is already being employed to extract copper from low grade ores), the petroleum polluted sites in the southern part of the country, and issues associates with animal husbandry and aquaculture.

Biotechnology programs less strongly aligned to industry sectors that could benefit included (1) biomass conversion, (2) the food industry, and (3) nutraceuticals and botanic drugs. These biotechnology programs were characterized by weak relationships with stakeholders, a lack of recognition by funding agencies, and an insufficient number of trained personnel. The ILB team met with two groups involved in biomass conversion, although only one appeared to be actively involved with biotechnological applications to these issues. The potential for the conversion of cellulosic material into ethanol is high. However the ILB group felt that the level of support was quite low. Considering that forestry supplies and potential expansion into marginal agricultural land in Chile is large and could support a significant level of bio-ethanol production, this should be carefully evaluated. Microalgae biodiesel research should be also be considered as a high priority especially as this industry which might be a good fit for the Northern desert regions and other areas of Chile with suitable climates. The IBL team recommends the evaluation of current research going on throughout the world rather than a de novo project.

Within the food industry, the functional food sector is expected to exhibit the most substantial growth. By 2013, it is estimated that the global functional food market is expected to reach a value of at least US$90.5 billion. Increasing consumer interest in the role of nutrition for health and wellbeing is a primary driver behind the success of the functional food market. Another market force is consumers' increasing desire to take a more proactive role in optimizing personal health and wellbeing, without relying on pharmaceuticals. ILB evaluated the role of biotechnology in the Chilean food industry in the areas of nutritional quality, ingredients, functional foods and probiotics. ILB did not review any Chilean biotechnology program specifically designated to improve the nutritional quality of foods. While this application is more limited than enhancing foods for specific health needs such as diabetes, it deserves consideration in those areas in which the research can be directly linked to stakeholder needs or the immediate improvement of Chilean exports. The identification of biologically active phytochemical ingredients plays a significant role in developing successful dietary supplements and functional foods. While several researchers presented general findings on antioxidant capabilities of native Chilean plants, specifics on novel compounds or extracts were not forthcoming.

Lack of novelty and the failure to identify new compounds from native plant species should not be viewed as a deterrent to the development of a vigorous ingredient or functional food industry. Rather, by adopting the latest molecular targets for

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screening, extracts standardization, use of whole cells assays and standardized animal models, it is possible to develop intellectual property (IP) on unique combinations of phytochemicals from standardized extracts of native plant species. In order to maximize efficiency of this program, ILB suggests a centralized screening facility housing both research and pilot plant extraction facilities. A pilot plant capable of supercritical fluid extraction is essential to the success of any program developing unique phytochemical ingredients and functional foods. Pilot plants produce marketing prototypes as well as the necessary testing materials for clinical trials. The exploration of the Chilean biodiversity for novel medicinal and agrochemical leads should be encouraged

Finally, there were those biotechnology programs unaligned to industry sectors that could benefit. Biomedicine was the most significant example of such a program. In spite of a large resource allocation, there is a minimal probability of success due to extremely competitive and well-funded global activity and a fundamental lack of relationship with the industry served. This is in general a highly competitive world market with enormous resources available through large pharmaceutical companies, government and non-profits agencies such as the National Institute of Health (NIH), National Science Foundation (NSF) the European Community (EC), the Gates Foundation and many others throughout North America, Europe and Japan. Since this sector is extremely competitive, any generally recognized significant area would have multiple players involved with considerable resources. Due to the complexity of the process with many hurdles to overcome in reality it is very difficult to make a unique discovery, which could lead to a profitable product. Return on investment could be via licensing with milestone and royalty payments although early stage discoveries will be highly discounted. In contrast, products in Phase II clinical trials and further clinical trials are likely to be very valuable ($100MM plus evaluations for such opportunities being reported for a variety of pharmaceuticals). Even given the high value of such products, this is an unlikely event and aiming for a more easily commercialized product with a more modest market has to be considered as both more practical and a safer use of limited resources. For these reasons the ILB team concluded that although there are a number of very talented scientists working in Chile in these areas, resources might be focused on more reasonable and relevant (to Chile) projects. The area of biomedicine should be de-emphasized except in very select areas, i.e., those in which there is a unique advantage to the research and development being performed locally and in alliance with international centers including the pharmaceutical industry. However, the ILB team supports the educational value of these programs. Expanding the workforce through medical research is an important outcome of these efforts. Leveraging the Chilean university education through foreign interactions is essential to avoid duplicating what has been done or is being done at other institutions.

CONCERNS

Serious obstacles exist that have a direct effect in the potential impact of biotechnology on the Chilean economy. A summary of those obstacles includes the following:

- It is of vital importance for the Chilean biotechnology industry that a clear regulatory framework for development and marketing of GMO products is in place.
- There appears to be to a lack of sufficiently trained scientific personnel to be fully integrated in research projects.

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- Program leaders tend to continue their mentor's line of research with little modifications and showing certain risk adversity regarding new research directions.
- There is serious duplication of research objectives, particularly in the areas of fruit and biomedicine leading to parallel, competing projects.
- There is not a culture among scientists and project leaders regarding the importance of protecting intellectual property.
- The key areas of biomass conversion (bio-energy, forestry, industrial waste, chemicals), foods & nutrition and natural products appear to be inadequately funded. There seems to be a lack of awareness regarding the need to import technology in some of these areas instead of investing in research for internal development.
- In all of Chile there are no pilot plant facilities for the food, nutrition and natural products industries.

STRATEGIC RECOMMENDATIONS

ILB focused its effort in assessing biotechnology programs in Chile based on their technical content and strategic fit with key Chilean industry sectors identified to ILB by the Cosejo Nacional para la Innovacion. ILB strategic recommendations are focused in the technical content of the programs reviewed, their business relevance and allocation of funds in support of the programs.

Technical Content - ILB believes that in general this is a good and competitive portfolio of biotechnology research projects. Nevertheless, a number of projects lack the technical and scientific merit required to meet criteria for funding.

- It is critical to have a rigorous, objective international peer review of project proposals for funding.
- ILB recommends a proactive scientific oversight of projects including international members who could consult with scientists and provide recommendations on the scientific progress, strategic direction and competitive activity. In addition, funding agencies and industry management should benefit from this oversight.
- Duplication of scientific effort must be avoided. It is in part the responsibility of funding agencies to make sure that this does not happens.
- It is recommended the creation of centralized lab facilities to rationalize access to high-cost capital laboratory equipment (sequencing, NMR, Mass Spectrometry, electron microscopy etc) and access to service laboratories.
- It is critical to build at least one pilot plant facility in support of food, nutrition, nutraceutical and botanical drugs development activities.
- Nanotechnology will play an important role in critical areas such as food and nutrition, biomedicine etc. It is important to incorporate this technology in the country biotechnology platforms through international collaborations, technology transfer and licensing.

Business - Business and market analysis of the different programs reviewed were not available or the project leaders interviewed did not have a good grasp of the subject. The few business and market projections presented to ILB were unrealistic or with limited assessment of the research and business competition, IP protection and a clear development and market strategy. Education of technical personnel and leaders could take place by creating entrepreneurial boot camps with industry to assist in

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identifying opportunities and awareness of unmet needs. There is little awareness regarding intellectual property matters among scientists and their project leaders. As a result of this, only a handful of patents have been filed. It is critical to create a culture of IP protection and establish an effective technology transfer and IP protection policy and the organizations in support of these endevours. The role of venture capital funds could play a critical role in developing a viable biotechnology industry in Chile. Venture capital funding could be aligned with efforts in establishing technology transfer units and work closely with established incubators. Chilean development agencies could play a key role in creating the necessary incentives for international venture funds for their establishment and operation in Chile.

Funding - The fruit and bio-mining biotechnology programs have a reasonable expectation of success. These two programs are strongly aligned with key industries in Chile and their success will produce a significant impact on these two sectors. Programs involved in food and nutrition, biomass conversion and nutraceuticals and botanical drugs are not strongly aligned with the industry sector in Chile. New biotechnology programs in these fields should be encouraged provided that they are more tightly connected with the respective industrial sector. It is recommended that in addition to the scientific merit, granting agencies allocate funds to biotechnology projects primarily based on probability of success and degree of connection with the respective industrial sectors. Based on the information provided to ILB, presently this is not the case. Among the more than 200 projects reviewed including the 22 selected for more detail discussions, Biomedicine was awarded more than half of the funds, Fruits received approximately one fourth of the funds, followed by Biomass Conversion, Food and Nutrition and Bio-mining.

It is recommended the creation of Biotechnology Centers closely aligned with industry sectors that could take full advantage of existing technological platforms, promote synergism among scientists, better allocation of resources, avoid duplication of efforts and operate under a more centralized management that is well connected with industry. The highest priority should be given to the creation of the following Centers: Fruit, Food and Nutrition, Biomass Conversion and Bio-mining.

Programs in biomedicine lack a strong alignment with the industry sector and do not posses the critical mass to be competitive on a world basis. It is recommended that some of these programs be integrated into the global biotechnology through international collaborations. One possible scenario is the creation of a Biomedicine Chile-California Center taking advantage of the recently signed Chile-California Program.

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A. INTRODUCTION

*Global Tendencies***

During the last two years, biotechnology has continued to make substantial progress having a direct impact in key economic sectors:

- Stem cell research continues delivering important breakthroughs
- Technology/platform companies have rebounded
- Large pharmaceuticals/agricultural/food companies buys into the biotechnology pipelines
- Personalized medicine makes progress: FDA recommends genetic tests for the first time
- Biofuels continue to grow
- Industrial biotechnology is now a reality:
  - Dupont bio-fiber “Sorona”, next Nylon
  - Dupont sales of industrial biotech products to reach $1billion in 2012
  - Novozyme enzyme reaches revenues of $1 billion/year
  - Chiral intermediates become a $500 million/year market
  - Numerous patents granted to the industrial biotechnology sector
- Agricultural biotechnology and animal health continued to show increase in acreage and new products
- Biotechnology industry raises almost $50B in capital

Biotechnology is expected to have a significant impact in several industry sectors in the near future. The following trends are predicted

- From a Human Genome Project to Personal Genome
- From “one size fits all” drugs to personalized medicine
- From treating sickness to preventing sickness
- From aging just happens to aging is manageable
- From food for survival to food for health & “wellness”
- From fossil fuels to alternative fuels (biomass conversion)
- From using oil feedstocks to biomass feedstocks for industrial production
- From unavailable local capital to global access
- From fully integrated business model to virtually integrated business

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- From local companies to global companies
- From US centric biotech to global industry

New Markets

The global transformation being effected by biotechnology will have a significant impact in creating or expanding new markets:

- Metabolic diseases (obesity/diabetes)
- Alzheimer's/memory
- Anti-infectives (antibiotic resistance, new infectious diseases)
- Wellness (preventive/predictive cure)
- USA ethanol plant construction explosion (113 in operation, 77 under construction to produce 12 billion gallons)
- 20% of corn crop today and large future increase going to ethanol
- 13% of soybeans going to biodiesel

The new markets involving biomass conversion will not only concentrate on biofuels. The chemical industry is posed to benefit from new technologies under development for biomass conversion:

- The $1 trillion chemical industry is expected to grow by more than $500 billion in the next ten years
- 50% of the growth will come from Biotechnology (biopolymers, paints, specialty chemicals, commodity chemicals, textile fibers, industrial products)
- Industrial biotech sales are estimated to be $100 billion by 2011 (biofuels projection is $72 billion)
- Ethylene: The most widely produced organic compound ($115 billion market). Sugar-cane derived “bio-ethylene” is a reality
- “Bio-route” will be economically viable at $60 barrel oil

Partnering Trends

- The biotechnology industry continues to negotiate in a position of strength, commanding significant upfront fees and co-development rights in the fields of pharmaceuticals, biomass conversion and industrial biotechnology.

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- Large pharmaceutical companies are turning to each other to access new compounds and share risk:
    - BMS-Pfizer: Co-development of Phase III and preclinical compounds
    - AZ-BMS: Co-developing Phase II diabetes compound
    - BMS-ImClone (Erbitux)
- Competition for key technologies and compounds:
    - RNA silencing (Roche - Alnylam)
    - Antibodies (GSK - GenMab)
    - Anti-infectives, anti-cancer, autoimmune diseases, metabolic syndrome, biomass conversion, enzymes etc.
- Increasing activity from emerging regional markets (India)
    - BMS licenses dermatology products to Ranbaxy in the US

Financial and Capital Markets

The global interconnected economy has created a situation where diseases, food and energy crisis know no borders requiring a global coordinated response. It will be extremely important to continue to implement regulatory harmonization for the approval of new drugs and protect food safety as well as the protection of intellectual property.

The global financial markets have created additional opportunities for companies to look outside their borders for financing. European companies participate on NASDAQ/NYSE, Chinese companies on NYSE and Americans companies on Euronext. Other markets have become available (Tokyo, Hong Kong, Dubai). The global transformation being effected by biotechnology will have a significant impact in creating or expanding new financial markets.

The present global financial downturn is having a direct impact in the availability of credit for emerging companies, and new investments from all sources. Under this environment, venture funds and others will most likely focus in providing financial support to companies that they had previously funded rather than making new investments.

Biotechnology Advances Future Scenarios

- Drug discovery “in silico” and adaptive trials in market place

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- Personal genome at a cost of $100? The original price tag was $2.7 billion
- Personalized health record (including genotype) on smart card. Walk-in clinics and "consumerization" of healthcare
- Wellness care: Pre-symptomatic diagnosis and preventive medicine. Products are a combination of diagnosis, delivery/device or prescription drug.
- Regenerative medicine ("spare body parts")
- Botanical drugs and nutraceuticals will continue to expand to play an important role
- Business models change: Today's large pharmaceutical companies are tomorrow's "distributors". They will continue to outsource innovation, development and manufacturing. Biotechnology companies will be virtually integrated
- Biofuels will move beyond "corn ethanol" in favor of C4 grasses, sugar cane, forestry species, agricultural residues and algae
- Industrial chemicals and specialty chemicals derived from biomass using improved microorganisms, new enzymes and chemical process
- Sugar cane productivity substantially increased using a genomic approach. "Glucose Economy" replaces "Oil Economy"? (Geopolitical factor?)
- New transgenic crops and fruits for "wellness" and health
- Functional foods widely available

** ***Source: Burrill & Company***

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B. METHODOLOGY

InterLink Biotechnologies (ILB) team of consultants conducted an in depth review of research and development programs in biotechnology related to key sectors of the Chilean industry. The review was conducted from December 1 through the 6, 2008 in Santiago.

Prior to travelling to Chile, ILB received the following information from the Consejo Nacional de Innovacion para la Competitividad ("CNIC") for initial review and planning purposes:

- "National Innovation Strategy for Competitiveness" Eduardo Bitran. President
- "Towards A National Innovation Strategy For Competitiveness" Volume II 2008 (Draft)
- Final Report from "Idea Consultora" entitled: "Estudio sobre el potencial de la industria biotecnológica como plataforma para aumentar la competitividad de los sectores productivos con potencial identificados en Chile" ("The Potential of the Biotechnology Industry as a Platform to Increase the Competiveness of Certain Economic Sectors in Chile")
- Spreadsheets listing more than 200 R&D programs supported by government agencies in the fields of Mining, Aquiculture, Fruits Industry, Poultry/Hog Industry, Food Industry, Biomedicine and Biomass Conversion. The listing provided the names of Universities and other agencies conducting research in life sciences related to biotechnology including names of key contacts, general area of research and specific projects.
- Partnering Opportunities for Applied Research in Biotechnology in Chile (CORFO, March 2007, 489 pages) This is a Directory of R&D activities in Chile related to biotechnology in the following fields: Biomedical, Food & Nutrition, Aquaculture & Marine, Agriculture, Environmental, Biofertilizers, Bioremediation, Enabling Gene Technologies and Bioinformatics, Fermentation and Bioprocesses
- Spreadsheet listing names and contact information of biotechnology companies, R&D Centers and other entities related to biotechnology

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- Other general non-technical promotional government publications or copies of public presentations related to biotechnology in Chile.

Together with information provided by ILB's official Chilean contacts from the Consejo de Innovacion the team found a number of previous reviews of the Chilean biotechnology industry which were helpful in providing additional background information, history and perspective (for example, C. Hernandez-Cuevas and P. D. T. Valenzuela (2004), Strategies to capture biotechnology opportunities in Chile, Electronic Journal of Biotechnology, 7, 189-205; V. Guerrero, Chile's supermodel, Bioentrepreneur, Nature Publishing Group, 10 November 2005; Anonymous, Chile shows promising new developments with genetically enhanced fruit, 14.4.2006, Gate2Biotech, South Moravian Innovation Center; V. Pinto, Chile: Biotechnology Industry, US Commercial Service, June 2006.)

ILB reviewed the background information provided and selected 23 Program Leaders for direct face-to-face interviews to discuss their research strategy and specific research projects under their direction. The total number of research projects evaluated during the face-to-face discussions exceeded 50 and included the following areas:

- Agriculture (fruits), nutrition/functional foods
- Biomass conversion (bio-fuels)
- Bio-mining
- Biomedicine and diagnostics, nutraceuticals and natural products

The following areas were not assessed in detail because limited or no information of specific projects were available in the original listing provided to ILB:

- Biomass conversion (industrial waste, new chemicals and products)
- Nutraceuticals and Botanical Drugs
- Functional Foods

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C. FINDINGS

As the ILB team met and interviewed the various biotechnology program leaders in Chile, they searched for specific factors separating programs with the potential of generating high returns on investment from those with lower or low potential returns. Two factors were considered likely delineators of potential success: (1) alignment with stakeholders or industrial sectors in Chile and (2) resource allocation. Resource allocation, which is often associated with success, was dismissed, as diverse biotechnology programs were funded at relatively similar levels. More obvious to the ILB team, however, was that the single greatest influence on return for research expenditure was the degree to which the biotechnological research was aligned to industry sectors in Chile that could directly benefit from the research effort. All interviewed programs were thus divided into one of three categories: (1) Biotechnology Strongly Aligned to Industry Sectors in Chile, (2) Biotechnology Less Strongly Aligned to Industry Sectors in Chile, and (3) Biotechnology Unaligned to Industry Sectors in Chile that Could Benefit.

The biotechnology programs strongly aligned to industry sectors included:

- Fruit industry
- Bio-mining

In these biotechnology programs, resource allocation appeared to have a significant, immediate impact in that they addressed important stakeholder problems and enabled continuous sector growth and global leadership. Thus, each sector had excellent return on investment potential.

Those biotechnology programs less strongly aligned to industry sectors that could benefit included:

- Biomass
- Food industry
- Nutraceuticals and botanic drugs

These biotechnology programs were characterized by weak relationships with stakeholders, a lack of recognition by funding agencies, and an insufficient number of trained personnel.

Finally, there were those biotechnology programs unaligned to industry sectors that could benefit. Biomedicine was the most significant example of such a program. In spite of a large resource allocation, there exists a minimal probability of success due to

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extremely competitive and well-funded global activity and lack of relationship with the industry served. Each of these three categories and industries are discussed in detail in the following sections.

Biotechnology Strongly Aligned to Industry Sectors in Chile

FRUIT INDUSTRY:

ILB conducted a review of six major programs involving a large number of research projects in fruit biotechnology. Several universities and research institutes are conducting this research with the support of state funding agencies and industry sectors through the participation in Consortia's. In general, the programs are sufficiently aligned with the needs and business strategies of the fruit sector (growers, processors and exporters) to enable the continuous growth and world leadership of this sector. Important problems such as the development of new proprietary varieties incorporating important input traits (disease resistance, drought tolerance, adaption to salinity etc) and key quality traits (post harvest and other quality traits) are being addressed applying biotechnology tools in combination with conventional breeding. Programs such as the genetic transformation of grapes and stone fruits and the related genomic programs associated with these species, should be considered as technology platforms that are a key requirement for the development of new products in support of the fruit industry

There is a need to allocate more resources to breeding programs supported by biotechnology tools (genetic markers etc.) The present breeding programs lack the required critical mass to make a significant impact in the industry, perpetuating the dependency on foreign varieties that not always meet the international market needs and local growing conditions. Research collaborations could be structured in such a way that provides for royalties to cooperators that provide access to technology with the option to use the genetic material to develop varieties in non-competing markets.

Further, there is duplication of efforts in several areas (grape transformation, genomic initiatives, disease resistance in grapes, quality trait genes in stone fruits and gene promoters in general). This duplication of efforts promotes unhealthy competition, which in turn becomes an obstacle to reach common objectives. Considering the magnitude of the effort, the size of the investment and the strategic importance of this

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technology for the fruit industry, ILB was surprised to learn that only a couple of patents have been filed to protect the intellectual property being generated.

BIO-MINING

This program has strong applications of basic microbiology and potential applications of biotechnology to mining industry issues. The use of natural isolates for the isolation of copper in low-grade ores is very promising and ILB looks forward to the full implementation of the industrial scale process and avoid diverting funds and efforts in pursuing new areas of research.

BIOREMEDIATION AND RELATED BIOTECHNOLOGY APPLICATIONS

Wood pulp industry - The ILB team was made aware of this problem although it was not discussed with any technical expert in Chile. The wood pulp industry in general has serious pollution problems on a global scale and any solution to the Chilean situation will be transferable to other sites (and obviously vice versa).

Typical wood pulp processing involves the use of large amounts of water and chlorine is used for bleaching for white paper production. The use of chlorine causes the production of toxic waste products such as dioxins and furans, and the waste water may also contain high levels of suspended solids, produce a high biological oxygen demand and either high or low pH values. This waste can be hazardous to human and marine life and underscores the importance of this issue.

Petroleum Pollutants and Heavy Metal Pollution - Biology plays a central role in the effective removal or neutralization of otherwise toxin organic and inorganic material. Biotechnological approaches employing microorganisms could be employed to address the following Chilean environmental problems; heavy metal pollution (biotechnology is already being employed to extract copper from low grade ores), the petroleum polluted sites of which there are more than two thousand in the southern part of the country, and issues associates with animal husbandry and aquaculture.

The use of bacteria and fungi in general for addressing heavy metal pollution has also been investigated internationally and there is considerable literature available. Without specific knowledge of the issues Chile faces in this area it is difficult for ILB to be

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more specific, but this seems to be a reasonable approach, which can be leveraged by the local biotechnology community to solve specific Chilean problems.

Petroleum pollution and oil spills have long been the target for using bioremediation, employing bacteria, fungi and vascular plants, although for Chile's purposes with multiple contaminated sites, the use of microorganisms may offer more flexibility. Again there is extensive literature available, for example *Bioremediation and its Application to Exxon Valdez Oil Spill in Alaska* written by Ray Gordon in 1994, and there are many bacteria and fungi, which have been shown to have the ability to degrade the various components of oil. There are many approaches to this problem which Chilean environmental microbiologists should be able to evaluate.

Wetlands - During the consulting meetings, the ILB team became aware of a single effort to use wetlands to remove undesirable pollutants and given the direct impact on the Chilean environment these efforts should be encouraged.

Biological bleaching - In addition the ILB team would like to propose that the use of biological bleaching be investigated. Certain Basidiomycetes, a type of fungus, for example have been shown to have the ability to bleach wood by decomposing the pigmented material. A small biotechnology company in North Carolina, AgraSol Inc, developed technology using bacteria and fungi, which had the ability to bleach wood, and this was introduced into the wood industry in the US. Similar operations may exist in other parts of the world's wood pulp industry.

This approach has the potential to reduce the level of toxic materials produced and should be investigated by Chilean biotechnology scientists; with the right effort this may be a workable solution with the potential to generate royalties by licensing the process to other countries.

Biotechnology Less Strongly Aligned to Industry Sectors in Chile

BIOMASS – Bioethanol and biodiesel

The ILB team met only two groups involved with biomass conversion. Only one group appeared to be actively involved in biotechnological applications trying to cover a broad range of research areas with limited funding. The potential for the conversion of

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cellulosic material into ethanol is high. However ILB felt that the level of support given to this area was quite low. Considering that forestry supplies and potential expansion into marginal agricultural land in Chile is large and could support a significant level of bioethanol production, this should be carefully evaluated. The biotechnological approach to converting biomass into sugars and ethanol has the advantage of being greener and will probably require much less capital expense for reactors than the traditional approaches using heat/acid based techniques.

On a global level there is a large amount of interest in the conversion of cellulosic material (e.g. wood) by cellulase enzymes produced by fungi as one example. The US Department of Energy has funded a number of projects in this area. A possible strategy could be to closely monitor developments of the technology around the world and establish licensing and strategic partnerships with the most suitable partners. This will require capabilities to follow and evaluate progress in other laboratories. A second strategy is to invest heavily in the basic research needed to bring the potential into reality. A small investment in developing technology is probably not going to create the critical mass needed to make a significant progress.

ILB was unable to fully evaluate other technologies presented to ILB such as converting biomass to gas but suggest that these are carefully examined to determine if public funding should be committed.

The microbial conversion of biomass could also be a source of commodity chemicals including the following: glycerol, 3 hydroxypropionic acid, aspartic, fumaric, malic, succinic, glutamic, itaconic and glucaric acids, xylitol, arabinitol and sorbitol (Top Value Added Chemicals from Biomass Volume 1; www.eere.energy.gov/). In addition, filamentous fungi, which have the ability to thrive on biomass, produce more than half of these compounds. A combination of metabolomics, genomics and proteomics, genetic engineering and fermentation could be applied to solve these problems in Chile through international collaborations and technology licensing.

The Microalgae biodiesel research ongoing at the Universidad of Concepcion should also be considered as a high priority especially as this industry might be a good fit for the Northern desert regions and other areas of Chile with suitable climates. The IBL team recommends the evaluation of current research going on throughout the world rather than a de novo project. However the evaluation of the algae collection from the

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University of Concepcion is a worthwhile project because it has the potential to leverage the algae collection at the university and there is a good possibility that new organisms will be discovered which could generate patentable intellectual property. A biotechnology approach to algal biofuels could be a good fit with Chilean geography, i.e., intense sunlight, land with limited use for other applications.

Research into the conversion of biomass into liquid fuels such as ethanol and butanol, and diesel from plants and algae is highly competitive. For example, in the US approximately three hundred million dollars was invested in algal biodiesel in 2008 alone. Because of this global competition it is recommended that Chilean researchers look for international collaborations to leverage their potentially valuable resources. Multiple uses for a single product may be possible and should be investigated. For example, micro algae could be a source of both diesel and proteins, as well as other nutrients, e.g., omega-3 fatty acids.

FOOD INDUSTRY

Within the food industry, the functional food sector is expected to exhibit the most substantial growth. By 2013, it is estimated that the global functional food market is expected to reach a value of at least US$90.5 billion. Increasing consumer interest in the role of nutrition for health and wellness is a primary driver behind the success of the functional food market. Another market force is consumers' increasing desire to take a more proactive role in optimizing personal health and wellness, without relying on pharmaceuticals. As consumer awareness in health continues to grow and develop, it means opportunities for new product development and marketing. Further, the market is also becoming globalized, and is no longer limited to more established food industries such as Western Europe and North America. Industry trends include: natural, whole and organic food, ingredients innovation and scientific support. The most popular functional foods by health concern will include ageing, cancer, diabetes, heart health and obesity.

Trends likely to shape the food industry over the next decade:

- Inherently Healthy: Consumers are increasingly choosing naturally healthy foods such as fruit, vegetables, salads, nuts and yogurt. Fruit is now USA's second-favorite snack.
- Grazing: Healthier snacks in vending machines, single-serving snacks, nutrition bars, diet bars, energy drinks and mineral waters are more commonly selected.

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- Low and Less: Low fat trumps low carbohydrate in what people seek in labels. Trans fats are on their way out. Demand for low calorie and light products will continue to grow. Soon to appear will be allergen-free claims on food labels.
- Doctoring Through Diet: Nearly two-thirds of shoppers tried to manage or treat a condition through diet. 72% of this effort addressed heart health. Next to low fat, whole grains were the most influential food label claim, influencing 62% of shoppers. Dairy products with cholesterol-lowering sterols, antioxidant-rich chocolate are making an appearance. Expect more functional foods to appear.
- People are choosing premium, gourmet foods. Fish, in particular, is undergoing something of a gourmet makeover.
- Quick Fix: People want less hassle in the kitchen. Easy to prepare and ready to eat are key ingredients. Expect more ultra-quick foods, bagged salads and side dishes.
- Drive-and Go: More people are ordering take-out from full-service restaurants. Take-out sales from these restaurants account for almost 10% of sales in the US. More than half of Americans eat this way during the week.
- Layering of Flavors: Flavored oils and vinegars, pairings of fruity and tangy flavors, Asian, Central American and Latin American flavors are in vogue.

It was with this background that ILB evaluated the role of biotechnology in the Chilean food industry in the areas of nutritional quality, ingredients, functional foods and probiotics.

Nutritional quality – The ILB team did not review any Chilean biotechnology program specifically designated to improve the nutritional quality of foods. While this application is more limited than enhancing foods for specific health needs such as diabetes, it deserves consideration in those areas in which the research can be directly linked to stakeholder needs or the immediate improvement of Chilean exports. One example of such a program would be increasing the omega 3 fatty acid content of salmon, as results of this research would directly benefit Chilean aquaculture.

Ingredients – The identification of biologically active phytochemical ingredients plays is a significant role in developing successful dietary supplements and functional foods, and is discussed in more detail in the *Functional foods* section.

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Functional foods – The Institute of Medicine's Food and Nutrition Board of the US National Science Foundation has defined functional foods as "any food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains." Most global research and food product development efforts have focused on plant products or phytochemicals. Chile has several special advantages for the development of Functional Foods. In no particular order these are (1) a dramatic range of climatic conditions for growing unique or custom crops, (2) a strong agricultural culture with global export experience, and (3) a long shoreline providing access to potentially novel ocean-based products.

During the ILB review, several researchers presented general findings on antioxidant capacity of native Chilean plants, specifics on novel compounds or extracts, however, were not forthcoming. The most successful attempt at the characterization of potential health benefit of a plant extract was the research on Murtilla leaves (*Ugni molinae Turcz*) as a source of antioxidant polyphenols. The antioxidant compounds identified (glycosilated myricetin and quercetin glycosides, epicatechin and gallic acid) are not novel as they are found in more common fruits, vegetables and teas. Anti-inflammatory compounds isolated from Murtilla leaves included betulinic acid, a mixture of ursolic and oleanolic acids, and the 2alpha-hydroxy derivatives of alphitolic, asiatic, and corosolic acids. Additionally, these triterpenoids and their anti-inflammatory activity are well characterized in the literature.

Lack of novelty and the failure to identify new compounds from native plant species should not be viewed as a deterrent to the development of a vigorous ingredient or functional food industry. Rather, by adopting the latest molecular targets for screening, extracts standardization, use of whole cells assays and standardized animal models, it is possible to develop intellectual property (IP) on unique combinations of phytochemicals from standardized extracts of native plant species. Short-term, clinical trials providing proof-of-concept for ingredients and functional foods addressing metabolic syndrome, type 2 diabetes, and cancer cachexia could also be conducted for products possessing appropriate IP protection.

In order to maximize efficiency of this program, ILB suggests a centralized screening facility housing both research and pilot plant extraction facilities. A pilot plant capable of supercritical fluid extraction is essential to the success of any program

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developing unique phytochemical ingredients and functional foods. Pilot plants produce marketing prototypes as well as the necessary testing materials for clinical trials.

Probiotics – ILB reviewed only one project in this field showing encouraging results in the application of cultures of natural bacteria on growth and infection control. ILB suggest that quantitative microbiology be conducted and the probiotics be compared to standard controls, e.g., antibiotics, against both natural infections and in animal models using gram positive and negative bacteria and fungi such as candida, and including antibiotic sensitive and resistant organisms. The IP position is probably weak but a local business might be a possibility.

Nutraceuticals and Botanical Drugs – The exploration of the Chilean biodiversity for novel medicinal and agrochemical leads should be encouraged. The biodiversity of the micro and macro organisms found in the Chilean terrestrial and marine environments must be considerable, and efforts should be made to document this, possibly through the use of sequencing of the microbial community. The use of modern bioactivity screening and natural products chemistry can quickly lead to new areas of unique research based on material available only within Chile. Collaborating with international natural products scientists in industry or academia especially those who have access to high field NMR and the latest mass spectrometers will accelerate these evaluations. The ILB team cautions against spending time rediscovering known compounds through the use of the best available de-replication techniques and commercial databases. The advantage to Chile is that new compounds can be protected through composition of matter patents.

The IBL team suggests that an inventory of the biodiversity within Chile including marine and terrestrial micro and macro organisms be conducted if it hasn't already been done. Following a discussion with members of CNIC science advisory board on Friday, December 5, the ILB team became aware of a project with Alan Bull in the UK to isolate actinomycetales from desert soil collected in the northern desert. It seems possible that the high exposure to uv radiation has resulted in high diversity of strains (it was also proposed that the source of unusual strains in the Ukraine following the Chernobyl accident was the release of ionizing radiation).

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Biotechnology Unaligned to Industry Sectors in Chile that Could Benefit

BIOMEDICINE

ILB recognizes that there are a number of talented scientists working in Chile who are generating exciting and interesting basic research data in biomedicine. However, this is a highly competitive world market with enormous resources available through large pharmaceutical companies, government and non-profits such as the National Institute of Health (NIH), National Science Foundation (NSF) the European Community (EC), the Gates Foundation and many others throughout North America, Europe and Japan. For these reasons, any generally recognized significant area would have multiple players involved with very significant resources available.

In reality it is very difficult to make a unique discovery, which could lead to a profitable product because of the complexity of the process with many hurdles to overcome. This process is risky and the chance of failure is high because of the subtle differences between the discovery and development procedure, which uses simple models early on, and then complex mammalian test and evaluation systems including human clinical trials. This is reflected in the high failure rate of medicinal discoveries, which is in excess of 99%. To discover new medicines requires significant resources of money and expertise, as well as access to clinical patients for trials. Outsourcing will be almost certainly needed to add to the capabilities observed.

Return on investment could be realized through licensing with milestone and royalty payments, although early stage discoveries are typically highly discounted. In contrast, products in Phase II clinical trials and closer to the market are likely to be very valuable with $100MM plus evaluations for such opportunities being reported for a variety of pharmaceuticals. Even given the high value of such products, this is an unlikely event and aiming for a more modest market has to be considered as both more practical and a safer use of limited resources.

In general and in light of the above constraints and the ILB team own experience with early stage medical opportunities, the group considered few of the projects would mature within the next decade, if at all, and may be considered less of an opportunity for a good return on investment than some of the other areas, e.g., fruits, nutrition, biomining and biofuels.

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For the reasons mentioned above the ILB team concluded that the area of biomedicine should be de-emphasized except in very select areas, i.e., those in which there is a unique advantage for the research and development to be performed locally. There seems to be strong scientific capabilities at the Universidad de Chile, Universidad Catolica and Fundacion Ciencia para la Vida that could be better utilized by being part of a larger international effort involving the pharmaceutical industry or national agencies such as the US National Institute of Health, Cancer Foundation, European Community and others. Certain technologies being developed could fit well into those programs, and as such, could be kept focused in something specific instead of broad objectives.

However, ILB supports the educational value of these programs, and expanding the workforce through medical research is an important product of these efforts. Leveraging the Chilean university education through foreign interactions is essential to avoid duplicating what has been done or is being done at other institutions.

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D. CONCERNS

Following is a list of concerns that ILB believes poses a serious obstacle for biotechnology to have a significant impact in Chile.

- It is of vital importance for the Chilean biotechnology industry that a clear regulatory framework for development and marketing of GMO products is in place. Programs in the fruit area are presently at the stage of field-testing. Due to the lack of a regulatory framework, product development and eventual commercialization will not be feasible.
- Based on ILB assessment it appears to be to a lack of sufficiently trained scientific personnel to be fully integrated in research projects. This shortage is corrected in part by the availability of undergraduate and graduate students to work in projects. It is expected that this situation will be corrected in the future as a result of the on going training effort supported by the funding agencies.
- During ILB technical discussions with project leaders who have worked in other laboratories outside of Chile, it was noticed a tendency to continue their mentor's line of research with little modification and showing certain adversity to take risk regarding new research directions. University and national policies could provide guidance in term of research priorities to be supported by funding agencies. There is also certain resistance to incorporate technology developed elsewhere or to consider licensing technology packages or some of their components.
- As noticed earlier, there is serious duplication of research objectives leading to parallel, competing projects. This is in part due to a failure to recognize competing research locally as well as globally. This situation is particularly serious among some fruit and biomedicine projects. In the fruit area there are several duplicating efforts in genetic transformation of grapes, genomic programs and disease resistance. In the biomedicine area several programs involving Alzheimer and cancer suffer from the same problem. In general the competing groups do not communicate with each other leading to lack of collaboration and poor utilization of resources. This problem could be corrected in part if the funding agencies are more vigilant in coordinating their activities.
- As discussed earlier, ILB has been left with a clear impression that there is not a culture among scientists and project leaders regarding the importance of

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protecting intellectual property. Of a total of more than 200 projects looked at ILB counted only a handful of international patent applications. The project leaders interviewed are in general not familiar with basic IP protection issues, patent law, licensing and the concept of freedom to operate. This is a serious issue that must be addressed without delay. The Chilean government is investing large sums of money in biotechnology research and runs the risk that a number of technologies under development will not be able to reach the market due to lack of patent protection and freedom to operate.

- There are important industrial areas that are recognized as key to Chile that appear to be inadequately funded. These areas are biomass conversion (bioenergy, forestry, industrial waste, chemicals), foods & nutrition and natural products. There seems to be a lack of awareness regarding the need to import technology in some of these areas instead of investing in research for internal development. Biomass conversion could be such a candidate.
- Lack of pilot plant facilities for the food, nutrition and natural products industries is a rate limiting and easily addressable problem.

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E. STRATEGIC RECOMMENDATIONS

ILB focused its effort in assessing biotechnology programs in Chile based on their technical content and strategic fit with key Chilean industry sectors identified to ILB by the Cosejo de Innovacion para la Competividad. ILB strategic recommendations are focused in the technical content, business relevance of the programs reviewed and allocation of funds in support of the programs.

TECHNICAL CONTENT

Based on the list of projects reviewed, ILB believes that in general this is a good and competitive portfolio of biotechnology research projects. Nevertheless, a number of projects lack the technical and scientific merit required to meet criteria for funding. It is critical to have a rigorous, objective international peer review of project proposals for funding. The review should include weighting of key criteria based on factors such as strategic fit, critical mass, degree of novelty, competitive position etc.

ILB recommends a proactive scientific oversight of projects including international members who could consult with scientists and provide recommendations on the scientific progress, strategic direction and competitive activity. In addition, funding agencies and industry management should benefit from this oversight.

Several important projects in the fruit and biomedicine areas are being carried by different groups and pursuing similar objectives in most cases with little or no communication between them. For obvious reasons, duplication of scientific effort must be avoided and it is in part the responsibility of funding agencies to make sure that this does not happens.

There is a need to rationalize access to high-cost capital laboratory equipment (sequencing, NMR, Mass Spectrometry, electron microscopy etc) and access to service laboratories. It is recommended the creation of centralized lab facilities for this purpose. In discussion with scientists in the food industry sector it was mentioned that Chile does not posses a single pilot plant in support of food, nutrition, nutraceutical and botanical drugs development activities. It is critical to build at least one pilot plant facility to serve this need.

ILB was not exposed to a single program involving nanotechnology. This technology will play an important role in several areas such as food and nutrition,

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biomedicine etc. It is important to incorporate this technology in the country biotechnology platforms through international collaborations, technology transfer and licensing.

BUSINESS

ILB tried to obtain some realistic business and market analysis of the different programs reviewed. With very few exceptions, the information was not available or the project leaders interviewed did not have a good grasp of the subject. The few business and market projections presented to ILB were unrealistic or with limited assessment of the research and business competition, IP protection and a clear development and market strategy. It would be important to continue to aggressively pursue the creation of networks of incubators, angels and VCs and to create more business awareness through education of scientists and project managers.

Education of technical personnel and leaders could take place by creating entrepreneurial boot camps with industry to assist in identifying opportunities and awareness of unmet needs.

The ILB review clearly shows that there is little awareness regarding intellectual property matters among scientists and their project leaders. As a result of this, only a handful of patents have been filed. It is critical to create a culture of IP protection and establish an effective technology transfer and IP protection policy and organizations in support of these endevours. It should be considered as high priority to strengthen the role or the creation of Technology Transfer and Commercialization Centers that could function as a conduit between research activities and the market place helping to create a more market driven focus and the creation of new business and companies.

The role of venture capital funds could play a critical role in developing a viable biotechnology industry in Chile. Venture capital funding could be aligned with efforts in establishing technology transfer units and work closely with established incubators. Chilean development agencies could play a key role in creating the necessary incentives for international venture funds for their establishment and operation in Chile.

It has been recognized that specialized scientific students have few of the skills needed for successful business; in part this is created by the need to study technical material in depth and the subsequent reluctance of the student to be distracted from this investment. This is a problem not unique to Chile. In the US, a member of the ILB team

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has been actively engaged in developing a new educational program for the North Carolina State University's program of biotechnology (*Industry Immersion Learning: Real-Life Industry Case-Studies in Biotechnology and Business* by Lisbeth Borbye, Michael Stocum, Alan Woodall, and Cedric Pearce. Wiley, Hardcover – to be published Mar 30, 2009). Students and staff perceive this as useful especially as the student moves into the industrial setting. The goal of developing an entrepreneur boot camp is to raise the awareness of scientifically trained researchers to opportunities for commercialization of their results, whether this is directly as a product, or in developing an enabling technology. This role could be assumed by the university business schools in Chile with the emphasis on enlightenment rather than providing a full MBA course. An abbreviated selection including intellectual property, market research, basic business plan as a route to sharing a vision, the start-up environment, structure and management of a new company would help in producing a more entrepreneurial culture.

FUNDING ALLOCATION

The fruit and bio-mining biotechnology programs have a reasonable expectation of success. These two programs are strongly aligned with key industries in Chile and their success will produce a significant impact on these two sectors.

Programs involved in food and nutrition, biomass conversion and nutraceuticals and botanical drugs are not strongly aligned with the industry sector in Chile. New biotechnology programs in these fields should be encouraged provided that they are more tightly connected with the respective industrial sector.

It is recommended that in addition to the scientific merit, granting agencies allocate funds to biotechnology projects primarily based on probability of success and degree of connection with the respective industrial sectors. Based on the information provided to ILB, presently this is not the case. Among the more than 200 projects reviewed including the 22 selected for more detail discussions, Biomedicine was awarded more than half of the funds, Fruits received approximately one fourth of the funds, followed by Biomass Conversion, Food and Nutrition and Biomining.

It is recommended the creation of Biotechnology Centers closely aligned with industry sectors that could take full advantage of existing technological platforms, promote synergism among scientists, better allocation of resources, avoid duplication and operate under a more centralized management that is well connected with industry.

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The highest priority should be given to the creation of the following Centers: Fruit, Food and Nutrition, Biomass Conversion and Bio-mining.

Programs in biomedicine lack a strong alignment with the industry sector and do not posses the critical mass to be competitive on a world basis. As mentioned above, it is recommended that some of these programs be integrated into the global biotechnology effort through international collaborations involving the pharmaceutical industry or national agencies such as the US National Institute of Health, Cancer Foundation, European Community and others. Certain technologies being developed could fit well into those programs, and as such, could be kept focused in something specific instead of broad objectives. One possible scenario discussed by one group, would be the creation of a Biomedicine Chile-California Center taking advantage of the recently signed Chile-California Program.

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SUMMARY

Founder and CEO of InterLink Biotechnologies LLC., a company established in 1991 and acquired by a large pharmaceutical company in September of 2003. InterLink Biotechnologies developed a unique drug discovery platform of novel natural products derived from microorganisms. Products resulting from the company activities include new pharmaceutical drugs, antimicrobial peptides, enzymes as additives for human food and animal feed products and bio-control agents.

Senior Manager Research & Development and CEO. More than twenty years experience in directing and leading research in the field of biotechnology with applications in pharmaceuticals, food, agriculture and chemicals. Responsible for starting and directing two major corporate biotechnology laboratories in the field of agricultural biotechnology. Proven accomplishments include the development of new products and technologies and the transfer and licensing of new technologies.

Demonstrated experience and accomplishments:

- Excellent management skills. Founded and developed successful biotechnology company that was lately acquired by a large pharmaceutical company
- Founded and manages two biotechnology companies in the field of agriculture
- Effectively built productive teams within a multi-disciplinary environment
- Designed, built, and staffed two biotechnology research centers
- Developed short and long term research strategies for two multinationals companies
- Developed new products and technologies that generated multimillion dollar revenues within a short time
- Direct involvement in the initiation of university contracts, technology joint ventures, licensing and acquisition of technologies
- Proven international experience. Worked for an international organization in a developing country and with two large multinationals
- Worked in numerous assignments involving technology assessments, strategic planning, and technology transfer for a number of international corporations and universities

- In conjunction with Fundacion Chile, established a biotechnology research program and a biotechnology company in Chile

PROFESSIONAL EXPERIENCE:

InterLink Associates, LLC. **2003 - Present**
President

InterLink Associates specializes in technology acquisition, licensing and transfer for the biotechnology and pharmaceutical industries. InterLink's possess in-depth scientific as well as business knowledge of the biotechnology industries resulting from more than 20 years of hands-on experience.

InterLink is an equity holder and manages two biotechnology companies in the field of agriculture: GenVitis S.A. (Chile) and Vitis Biosciences, Inc. in the USA.

InterLink Biotechnologies, LLC **1991 - 2003**
President & CEO

InterLink Biotechnologies developed a unique drug discovery platform of novel natural product derived from microorganisms. Products resulting from the company activities include new pharmaceutical drugs, antimicrobial peptides enzymes as additives for human food and animal feed products and bio-control agents.

- Founded and develop the company and built a strong technology platform for drug discovery.

- Established strategic alliances and collaborations with several pharmaceutical and biotechnology companies.

- Managed and directed all the company operations including a research center in California.

- Successfully sold the company to a large pharmaceutical company in 2003.

EniChem America, Inc. **1986 - 1991**
Corporate Research and Development
EniChem is a $12 billion chemical conglomerate based in Milan, Italy.
Director of Biotechnology Center

Directed the start up of EniChem's Biotechnology Center, a multi-disciplinary research facility with activities in Biotechnology for the development of genetically engineered products for the agriculture and food industries.

Significant accomplishments include:

- Set up a balanced research strategy that developed technologies in the short term and generated multimillion dollar income.

- Staffed 70 scientists (32 Ph.D.) in a short time (18 months).
- Designed and equipped a new 50,000 SF multimillion dollar laboratory facility.
- Developed operating and administrative procedures for the new EniChem Research Center.
- Responsible for overall budgetary ($10 MM/year), personnel and administrative functions.
- Established collaborative and contract research programs with universities and research institutes in the USA and Europe.
- Acquired, licensed in, and established research joint ventures in key technologies.
- Successfully transferred key technologies, know how, and assets to 6 major seed and agricultural chemical companies. Technologies transferred: Transformation, Gene Expression, Disease and Insect Resistance, and Urease Inhibitors.

Allied-Signal Corporation **1982 - 1986**
Corporate Technology

Director, Corporate Laboratory

Directed Allied's Biotechnology Program involving activities in basic and applied research for the development of products and technologies for the agriculture and food industries.

Significant accomplishments include:

- Started Allied-Signal biotechnology program.
- Staffed, designed, and equipped laboratory facilities.
- Planned and implemented and R&D strategy that included the commercialization of new technologies. Commercial activities were pursued through the acquisition of the Nitrogin Company, which became an Allied subsidiary.
- Other duties included overall budgetary, personnel (60 scientist), university relations and general administrative responsibilities.

Allied-Signal Corporation **1980 - 1982**
Chemical Company

Manager, R&D, Agricultural Products

Significant accomplishments include:

- Responsible for starting a new Research Program in Agricultural Chemicals.

- Developed research strategy and staffing of 55 scientists
- Set up and equipped laboratory facilities
- Coordinated research contracts with 20 universities and numerous outside contractors and field operations.

Allied-Signal Corporation **1975 - 1976**
Agricultural Division

Manager Product Development

Significant accomplishments include:

- Responsible for technical support to the Division's product line and development of new products
- Developed foliar fertilizers and micronutrients
- Extensive field testing and direct contact with university extension personnel, cooperators, and growers

EDUCATION

Ph.D., Iowa State University 1976
M.S., Iowa State University 1972

CURRICULUM VITAE

John G. Babish

Chairperson, Bionexus, Ltd.
Consultant on Signal Transduction Mechanisms of Xenobiotics
Consultant on Cornell Technology Transfer

Education

Institution and Location	Degree	Date Conferred	Field of Study
The Pennsylvania State University, State College, PA	B.S.	1968	Biochemistry
Cornell University, Ithaca, NY	M.S.	1974	Chemistry
Cornell University, Ithaca, NY	Ph.D.	1976	Biochemistry

Research and Professional Experience

Oct 2004 – present — Consultant to the dietary supplement and pharmaceutical industries in the areas of inflammation, metabolic syndrome, diabetes, cancer and AIDS. Bionexus laboratory performs contract research specializing in obesity, diabetes, inflammation and related cardiovascular diseases. Development of data for patent-protection of novel, nutritional products serving unmet health needs.

Dec. 1999 – 2004 — Co-founder and Executive Vice President of Research & Development, Ashni Naturaceuticals, Research Laboratories, Ithaca, NY. Ashni Naturaceuticals development of high quality, clinically proven patented dietary supplements and pharmaceuticals from natural sources. Duties included the design and evaluation of experiments elucidating mechanism of action and biological activity within complex mixtures. Intellectual property developed by Ashni has been licensed to companies in the dietary supplement industry.

1998 – present — (15% Effort) National Coordinator for the USDA Minor Species Drug Program (NRSP-7). The NRSP-7 program is funded by the USDA to provide funds and expertise necessary for the approval of pharmaceuticals used in the treatment of diseases associated with minor crop species. Duties include the coordination of industrial, academic and regulatory resources necessary for protocol development through final drug approval.

1997 – present — Co-founder and Chairperson of Bionexus, Ltd. Ithaca, NY. Bionexus develops and markets nutritional supplements to address health problems associated with AIDS. NutriVir™, the Bionexus supplement for wasting in HIV/AIDS, generated approximately $600,000 in gross revenues in its first year of sales. NutriVir™ is reimbursed by Medicaid in 14 states.

1991 – 1996 — Founder, Chairperson, President and CEO of Paracelsian, Inc., Ithaca, NY. The Company was launched from the technology transfer program of Cornell University in 1991, and with the public offering in 1992 (NASDAQ, PRLN), became the first public corporation of a Cornell University technology transfer effort. Babish was associated with the attainment of over $12 million dollars in corporate financing.

1984 – 1996 — Tenured Professor of Pharmacology and Toxicology, Department of Pharmacology, College of Veterinary Medicine, Cornell University. Offered the first course in molecular risk assessment in the USA in 1979; member of the graduate Fields of Pharmacology, Toxicology, Veterinary Medicine, Food Science and Epidemiology; successfully petitioned the State of New York for the approval of the separate Fields of Toxicology and Pharmacology at Cornell University.

1978 – 1984 — Assistant Professor, Department of Preventive Medicine, NYS College of Veterinary Medicine, Cornell University, Ithaca, NY.

1976 – 1978 — Postdoctoral Scientist, Food and Drug Research Labs, Waverly, NY.

Invited Presentations (Representative of 40)

Minor Use, Minor Species Research – Species Grouping. FDA/CVM Workshop Minor-Use and Minor Species: A Global Perspective. October 7th and 8th, 2004 Rockville, MD.

Micronutrient deficiencies in AIDS wasting at Progressive Management of AIDS Wasting: 2000. Hunter College, NYC. March 24, 2000.

Phytochemicals and NF-kB activation at IBC's Conference on The Health Benefits of Natural Phytoceuticals. Montreal Bonaventure Hilton, July 22 – 23, 1997.

Chemically-induced cell cycle stasis in immunotoxicology. 12th Annual NIOSH Conference on Mechanisms of Immunotoxicology – Role of Apoptosis in Immunotoxicology. University of West Virginia, Morgantown, WV. September 10 – 12, 1997.

Abstracts Presented at Scientific Meetings (126)

Peer-reviewed Publications

(1) Topic Popovic, N., Babish, J. G., and Bowser, P. R. (2007) Observational study of hepatic cytochrome P-450 protein expression and activity in summer flounder (Paralichtys dentatus) after combination ormetoprim-sulfadimethoxine treatment. *Chemotherapy 53*, 313-5.

(2) Hall, A. J., Tripp, M., Howell, T., Darland, G., Bland, J. S., and Babish, J. G. (2006) Gastric mucosal cell model for estimating relative gastrointestinal toxicity of non-steroidal anti-inflammatory drugs. *Prostaglandins Leukot Essent Fatty Acids 75*, 9-17.

(3) Payne, M. A., Babish, J. G., Bulgin, M., Lane, M., Wetzlich, S., and Craigmill, A. L. (2002) Serum pharmacokinetics and tissue and milk residues of oxytetracycline in goats following a single intramuscular injection of a long-acting preparation and milk residues following a single subcutaneous injection. *J Vet Pharmacol Ther 25*, 25-32.

(4) Calabrese, C., Berman, S. H., Babish, J. G., Ma, X., Shinto, L., Dorr, M., Wells, K., Wenner, C. A., and Standish, L. J. (2000) A phase I trial of andrographolide in HIV positive patients and normal volunteers. *Phytother Res 14*, 333-8.

(5) Stoffregen, D. A., Wooster, G. A., Bustos, P. S., Bowser, P. R., and Babish, J. G. (1997) Multiple route and dose pharmacokinetics of enrofloxacin in juvenile Atlantic salmon. *J Vet Pharmacol Ther 20*, 111-23.

(6) Rininger, J. A., Stoffregen, D. A., and Babish, J. G. (1997) Murine hepatic p53, RB, and CDK inhibitory protein expression following acute 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Chemosphere 34*, 1557-68.

(7) Rininger, J. A., Goldsworthy, T. L., and Babish, J. G. (1997) Time course comparison of cell-cycle protein expression following partial hepatectomy and WY14,643-induced hepatic cell proliferation in F344 rats. *Carcinogenesis 18*, 935-41.

(8) Ma, X., Stoffregen, D. A., Wheelock, G. D., Rininger, J. A., and Babish, J. G. (1997) Discordant hepatic expression of the cell division control enzyme p34cdc2 kinase, proliferating cell nuclear antigen, p53 tumor suppressor protein, and p21Waf1 cyclin-dependent kinase inhibitory protein after WY14,643 ([4-chloro-6-(2,3-xylidino)-2-pyrimidinylthio]acetic acid) dosing to rats. *Mol Pharmacol 51*, 69-78.

(9) Vancutsem, P. M., and Babish, J. G. (1996) In vitro and in vivo study of the effects of enrofloxacin on hepatic cytochrome P-450. Potential for drug interactions. *Vet Hum Toxicol 38*, 254-9.

(10) Sweeney, L. M., Shuler, M. L., Quick, D. J., and Babish, J. G. (1996) A preliminary physiologically based pharmacokinetic model for naphthalene and naphthalene oxide in mice and rats. *Ann Biomed Eng 24*, 305-20.

(11) Rininger, J. A., Wheelock, G. D., Ma, X., and Babish, J. G. (1996) Discordant expression of the cyclin-dependent kinases and cyclins in rat liver following acute administration of the hepatocarcinogen [4-chloro-6-(2,3-xylidino)-2-pyrimidinylthio] acetic acid (WY14,643). *Biochem Pharmacol 52*, 1749-55.

(12) Trepanier, L. A., and Babish, J. G. (1995) Pharmacokinetic properties of bromide in dogs after the intravenous and oral administration of single doses. *Res Vet Sci 58*, 248-51.

(13) Trepanier, L. A., and Babish, J. G. (1995) Effect of dietary chloride content on the elimination of bromide by dogs. *Res Vet Sci 58*, 252-5.

(14) Snow, R., Babish, J. D., and McBean, A. M. (1995) Is there any connection between a second pneumonia shot and hospitalization among Medicare beneficiaries? *Public Health Rep 110*, 720-5.

(15) Mufti, N. A., Bleckwenn, N. A., Babish, J. G., and Shuler, M. L. (1995) Possible involvement of the Ah receptor in the induction of cytochrome P-450IA1 under conditions of hydrodynamic shear in microcarrier-attached hepatoma cell lines. *Biochem Biophys Res Commun 208*, 144-52.

(16) Monticello, T. M., Barton, D., Ma, X., Babish, J. G., and Durham, S. K. (1995) Comparison of acute hepatocellular proliferating cell nuclear antigen labeling indices and growth fractions, p34cdc2 kinases,

and serum enzymes in carbon tetrachloride-treated rats. *Toxicol Pathol 23*, 439-46.
(17) Warren, J. L., McBean, A. M., Hass, S. L., and Babish, J. D. (1994) Hospitalizations with adverse events caused by digitalis therapy among elderly Medicare beneficiaries. *Arch Intern Med 154*, 1482-7.
(18) DeVito, M. J., Ma, X., Babish, J. G., Menache, M., and Birnbaum, L. S. (1994) Dose-response relationships in mice following subchronic exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin: CYP1A1, CYP1A2, estrogen receptor, and protein tyrosine phosphorylation. *Toxicol Appl Pharmacol 124*, 82-90.
(19) Vancutsem, P. M., and Babish, J. G. (1993) Effects of ciprofloxacin and enrofloxacin on zoxazolamine kinetics, plasma concentration and sleeping times in mice. *Toxicol Lett 69*, 1-14.
(20) Ma, X., and Babish, J. G. (1993) Acute 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure results in enhanced tyrosylphosphorylation and expression of murine hepatic cyclin dependent kinases. *Biochem Biophys Res Commun 197*, 1070-7.
(21) Eltom, S. E., Babish, J. G., and Schwark, W. S. (1993) The postnatal development of drug-metabolizing enzymes in hepatic, pulmonary and renal tissues of the goat. *J Vet Pharmacol Ther 16*, 152-63.
(22) Weng, Y. M., Hotchkiss, J. H., and Babish, J. G. (1992) N-nitrosamine and mutagenicity formation in Chinese salted fish after digestion. *Food Addit Contam 9*, 29-37.
(23) Ma, X. F., Babish, J. G., Scarlett, J. M., Gutenmann, W. H., and Lisk, D. J. (1992) Mutagens in urine sampled repetitively from municipal refuse incinerator workers and water treatment workers. *J Toxicol Environ Health 37*, 483-94.
(24) Ma, X., Mufti, N. A., and Babish, J. G. (1992) Protein tyrosine phosphorylation as an indicator of 2,3,7,8-tetrachloro-p-dioxin exposure in vivo and in vitro. *Biochem Biophys Res Commun 189*, 59-65.
(25) Gibbons, J. A., and Babish, J. G. (1992) Benzo[e]pyrene elicits changes in the biochemical activities and chromatographic behavior of murine hepatic cytochromes P-450 that are distinct from those induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chem Biol Interact 83*, 203-20.
(26) Eltom, S. E., Babish, J. G., and Ferguson, D. C. (1992) The interaction of L-triiodothyronine and 2,3,7,8-tetrachlorodibenzo-p-dioxin on Ah-receptor-mediated hepatic Phase I and Phase II enzymes and iodothyronine 5'-deiodinase in thyroidectomized rats. *Toxicol Lett 61*, 125-39.
(27) Bowser, P. R., Wooster, G. A., St Leger, J., and Babish, J. G. (1992) Pharmacokinetics of enrofloxacin in fingerling rainbow trout (Oncorhynchus mykiss). *J Vet Pharmacol Ther 15*, 62-71.
(28) Ma, X. F., Gibbons, J. A., and Babish, J. G. (1991) Benzo[e]pyrene pretreatment of immature, female C57BL/6J mice results in increased bioactivation of aflatoxin B1 in vitro. *Toxicol Lett 59*, 51-8.
(29) LaLonde, R. T., Cook, G. P., Perakyla, H., Dence, C. W., and Babish, J. G. (1991) Salmonella typhimurium (TA100) mutagenicity of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone and its open- and closed-ring analogs. *Environ Mol Mutagen 17*, 40-8.
(30) Javitt, J. C., McBean, A. M., Nicholson, G. A., Babish, J. G., Warren, J. L., and Krakauer, H. (1991) Undertreatment of glaucoma among black Americans. *N Engl J Med 325*, 1418-22.
(31) Broome, R. L., Brooks, D. L., Babish, J. G., Copeland, D. D., and Conzelman, G. M. (1991) Pharmacokinetic properties of enrofloxacin in rabbits. *Am J Vet Res 52*, 1835-41.
(32) Bowser, P. R., and Babish, J. G. (1991) Enrofloxacin in salmonids. *Vet Hum Toxicol 33 Suppl 1*, 46-8.
(33) Babish, J. G., Scarlett, J. M., Voekler, S. E., Gutenmann, W. H., and Lisk, D. J. (1991) Urinary mutagens in cosmetologists and dental personnel. *J Toxicol Environ Health 34*, 197-206.
(34) Vancutsem, P. M., Babish, J. G., and Schwark, W. S. (1990) The fluoroquinolone antimicrobials: structure, antimicrobial activity, pharmacokinetics, clinical use in domestic animals and toxicity. *Cornell Vet 80*, 173-86.
(35) Scarlett, J. M., Babish, J. G., Blue, J. T., Voekler, S. E., and Lisk, D. J. (1990) Urinary mutagens in municipal refuse incinerator workers and water treatment workers. *J Toxicol Environ Health 31*, 11-27.
(36) Babish, J. G., Coles, G. C., Tritschler, J. P., 2nd, Gutenmann, W. H., and Lisk, D. J. (1990) Toxicity and tissue residue depletion of levamisole hydrochloride in young goats. *Am J Vet Res 51*, 1126-30.
(37) Trotter, E. J., Crissman, J., Robson, D., and Babish, J. (1988) Influence of nonbiologic implants on laminectomy membrane formation in dogs. *Am J Vet Res 49*, 634-43.
(38) Rashid, K. A., Babish, J. G., and Mumma, R. O. (1988) In vitro activation assays with hepatic S9 preparation from wild and laboratory reared woodchucks in the Salmonella mutagenicity test. *Toxicology 48*, 53-9.
(39) Shoaf, S. E., Schwark, W. S., Guard, C. L., and Babish, J. G. (1987) The development of hepatic drug-metabolizing enzyme activity in the neonatal calf and its effect on drug disposition. *Drug Metab Dispos 15*, 676-81.
(40) Scarlett-Kranz, J. M., Babish, J. G., Strickland, D., and Lisk, D. J. (1987) Health among municipal sewage and water treatment workers. *Toxicol Ind Health 3*, 311-9.
(41) Durham, S. K., Babish, J. G., and Castleman, W. L. (1987) 4-Ipomeanol-induced effects on Sendai

viral pneumonia in mice. *Am J Pathol 126*, 364-75.
(42) Conzelman, G. M., Babish, J. G., Davidson, J. N., McMillan, R. A., and Copeland, D. D. (1987) Pharmacokinetics of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(4-ethyl-1-piperazinyl)-3-q uinoline-carboxylic acid (BAY Vp 2674) in chickens. *Proc West Pharmacol Soc 30*, 393-5.
(43) Stoewsand, G. S., Babish, J. G., Telford, J. N., Bahm, C., Bache, C. A., Gutenmann, W. H., and Lisk, D. J. (1986) Response of Japanese quail fed seed meal from sunflowers grown on a municipal sludge-amended soil: elevation of cadmium in tissues. *J Toxicol Environ Health 17*, 91-100.
(44) Scarlett-Kranz, J. M., Babish, J. G., Strickland, D., Goodrich, R. M., and Lisk, D. J. (1986) Urinary mutagens in municipal sewage workers and water treatment workers. *Am J Epidemiol 124*, 884-93.
(45) Milligan, D. L., Babish, J. G., and Neuhauser, E. F. (1986) Noninducibility of cytochrome P-450 in the earthworm Dendrobaena veneta. *Comp Biochem Physiol C 85*, 85-7.
(46) Brooks, B. A., Wassom, D. L., and Babish, J. G. (1986) H-2 modulation of aryl hydrocarbon hydroxylase induction and the mutagenicity of benzo(a)pyrene after 3-methylcholanthrene treatment. *Adv Exp Med Biol 197*, 797-807.
(47) Rashid, K. A., Baldwin, I. T., Babish, J. G., Schultz, J. C., and Mumma, R. O. (1985) Mutagenicity tests with gallic and tannic acid in the Salmonella/mammalian microsome assay. *J Environ Sci Health B 20*, 153-65.
(48) Rashid, K. A., Babish, J. G., Johnson, B. E., and Mumma, R. O. (1985) Comparative mutagenicity tests in the Salmonella/microsome assay with rat and woodchuck S9 preparations. *Toxicology 36*, 139-46.
(49) McLain, D. E., Harper, S. M., Roe, D. A., Babish, J. G., and Wilkinson, C. F. (1985) Congenital malformations and variations in reproductive performance in the ferret: effects of maternal age, color and parity. *Lab Anim Sci 35*, 251-5.
(50) McLain, D. E., Babish, J. G., and Roe, D. A. (1985) Pharmacokinetics of ethanol in the ferret. *Alcohol Clin Exp Res 9*, 138-42.
(51) Kemen, M. J., Frank, R. A., and Babish, J. B. (1985) An outbreak of equine influenza at a harness horse racetrack. *Cornell Vet 75*, 277-88.
(52) Frederick, K. A., and Babish, J. G. (1985) Compendium of recent literature on the ferret. *Lab Anim Sci 35*, 298-318.
(53) Telford, J. N., Babish, J. G., Johnson, B. E., Thonney, M. L., Currie, W. B., Bache, C. A., Gutenmann, W. H., and Lisk, D. J. (1984) Toxicologic studies with pregnant goats fed grass-legume silage grown on municipal sludge-amended subsoil. *Arch Environ Contam Toxicol 13*, 635-40.
(54) Telford, J. N., Babish, J. G., Dunham, P. B., Hogue, D. E., Miller, K. W., Stoewsand, G. S., Magee, B. H., Stouffer, J. R., Bache, C. A., and Lisk, D. J. (1984) Toxicologic studies with lambs fed sugar beets grown on municipal sludge-amended soil: lowered relative hemoglobin in red blood cells and mutagens in blood and excreta. *Am J Vet Res 45*, 2490-4.
(55) Stoewsand, G. S., Anderson, J. L., Boyd, J. N., Hrazdina, G., Babish, J. G., Walsh, K. M., and Losco, P. (1984) Quercetin: a mutagen, not a carcinogen, in Fischer rats. *J Toxicol Environ Health 14*, 105-14.
(56) Rashid, K. A., Babish, J. G., and Mumma, R. O. (1984) Testing of 2,4,5-T-amino acid conjugates for mutagenic activity in Salmonella typhimurium strains. *Mutat Res 136*, 217-21.
(57) Rashid, K. A., Babish, J. G., and Mumma, R. O. (1984) Potential of 2,4-dichlorophenoxyacetic acid conjugates as promutagens in the Salmonella/microsome mutagenicity test. *J Environ Sci Health B 19*, 689-701.
(58) Patton, W. H., Schwartz, L. D., Babish, J. G., and Lisk, D. J. (1984) Use of amprolium for the control of coccidiosis in pheasants. *Avian Dis 28*, 693-9.
(59) Frederick, K. A., and Babish, J. G. (1984) In vitro activation of the promutagens 2-acetamidofluorene, cyclophosphamide and 7,12-dimethylbenzanthracene by constitutive ferret and rat hepatic S-9 fractions. *Toxicology 31*, 73-86.
(60) Cottrell, W. O., Ringer, R. K., and Babish, J. G. (1984) Acute toxicity of dietary polybrominated biphenyls in Bobwhite quail. *Bull Environ Contam Toxicol 33*, 308-12.
(61) Babish, J. G., Stoewsand, G. S., Kranz, J. M., Boyd, J. N., Ahrens, V. D., and Lisk, D. J. (1984) Toxicologic studies associated with the agricultural use of municipal sewage sludge and health effects among sewage treatment plant workers. *Regul Toxicol Pharmacol 4*, 305-21.
(62) Wassom, D. L., Brooks, B. O., Babish, J. G., and David, C. S. (1983) A gene mapping between the S and D regions of the H-2 complex influences resistance to Trichinella spiralis infections of mice. *J Immunogenet 10*, 371-8.
(63) Wagner, J. G. (1983) Significance of ratios of different volumes of distribution in pharmacokinetics. *Biopharm Drug Dispos 4*, 263-70.
(64) Skrabalak, D. S., and Babish, J. G. (1983) Safety standards for occupational exposure to

dichloromethane. *Regul Toxicol Pharmacol 3*, 139-43.
(65) Ponnampalam, R., Mondy, N. I., and Babish, J. G. (1983) A review of environmental and health risks of maleic hydrazide. *Regul Toxicol Pharmacol 3*, 38-47.
(66) Parent, R. A., Re, T. A., Babish, J. G., Cox, G. E., Voss, K. A., and Becci, P. J. (1983) Reproduction and subchronic feeding study of carnauba wax in rats. *Food Chem Toxicol 21*, 89-93.
(67) Parent, R. A., Cox, G. E., Babish, J. G., Gallo, M. A., Hess, F. G., and Becci, P. J. (1983) Subchronic feeding study of carnauba wax in beagle dogs. *Food Chem Toxicol 21*, 85-7.
(68) Hang, Y. D., Babish, J. G., Bache, C. A., and Lisk, D. J. (1983) Fate of cadmium and mutagens in municipal sludge-grown sugar beets and field corn during fermentation. *J Agric Food Chem 31*, 496-9.
(69) Becci, P. J., Hess, F. G., Gallo, M. A., Johnson, W. D., and Babish, J. G. (1983) Subchronic feeding study of grape colour extract in beagle dogs. *Food Chem Toxicol 21*, 75-7.
(70) Becci, P. J., Hess, F. G., Babish, J. G., Gallo, M. A., and Voss, K. A. (1983) Reproduction study of grape colour extract in rats. *Food Chem Toxicol 21*, 79-83.
(71) Babish, J., Gal'chin, V. V., Stazhadze, L. L., and Bogomolov, V. V. (1983) [Method of identifying the peridural space]. *Anesteziol Reanimatol*, 63-4.
(72) Telford, J. N., Thonney, M. L., Hogue, D. E., Stouffer, J. R., Bache, C. A., Gutenmann, W. H., Lisk, D. J., Babish, J. G., and Stoewsand, G. S. (1982) Toxicologic studies in growing sheep fed silage corn cultured on municipal sludge-amended acid subsoil. *J Toxicol Environ Health 10*, 73-85.
(73) Litten, S., Babish, J. G., Pastel, M., Werner, M. B., and Johnson, B. (1982) Relationship between fluorescence of polynuclear aromatic hydrocarbons in complex environmental mixtures and sample mutagenicity. *Bull Environ Contam Toxicol 28*, 141-8.
(74) Lisk, D. J., Boyd, R. D., Telford, J. N., Babish, J. G., Stoewsand, G. S., Bache, C. A., and Gutenmann, W. H. (1982) Toxicologic studies with swine fed corn grown on municipal sewage sludge-amended soil. *J Anim Sci 55*, 613-9.
(75) Grieve, R. B., Brooks, B. O., Babish, J. G., Jacobson, R. H., and Cypess, R. H. (1982) Lymphocyte function in experimental canine dirofilariasis: B-cell responses to heterologous antigen. *J Parasitol 68*, 341-3.
(76) Frederick, K. A., and Babish, J. G. (1982) Evaluation of mutagenicity and other adverse effects of occupational exposure to sodium azide. *Regul Toxicol Pharmacol 2*, 308-22.
(77) Davidson, J. N., Babish, J. G., and Dunny, G. M. (1982) Bovine mastitis: antimicrobial resistance patterns. *J Am Vet Med Assoc 180*, 153-5.
(78) Davidson, J. N., and Babish, J. G. (1982) Clinical use of odds ratios in selecting antimicrobial therapy for bovine Pasteurella pneumonia. *Am J Vet Res 43*, 922-3.
(79) Boyd, J. N., Stoewsand, G. S., Babish, J. G., Telford, J. N., and Lisk, D. J. (1982) Safety evaluation of vegetables cultured on municipal sewage sludge-amended soil. *Arch Environ Contam Toxicol 11*, 399-405.
(80) Boyd, J. N., Babish, J. G., and Stoewsand, G. S. (1982) Modification of beet and cabbage diets of aflatoxin B1-induced rat plasma alpha-foetoprotein elevation, hepatic tumorigenesis, and mutagenicity of urine. *Food Chem Toxicol 20*, 47-52.
(81) Babish, J. G., Johnson, B., Brooks, B. O., and Lisk, D. J. (1982) Acute toxicity of organic extracts of municipal sewage sludge in mice. *Bull Environ Contam Toxicol 29*, 379-84.
(82) Dolinsky, Z. S., Burright, R. G., Donovick, P. J., Glickman, L. T., Babish, J., Summers, B., and Cypess, R. H. (1981) Behavioral effects of lead and Toxocara canis in mice. *Science 213*, 1142-4.
(83) Boyd, J. N., Misslbeck, N., Babish, J. G., Campbell, T. C., and Stoewsand, G. S. (1981) Plasma alpha-fetoprotein elevation and mutagenicity of urine as early predictors of carcinogenecity in benzo(alpha)pyrene fed rats. *Drug Chem Toxicol 4*, 197-205.
(84) Becci, P. J., Hess, F. G., Johnson, W. D., Gallo, M. A., Babish, J. G., Dailey, R. E., and Parent, R. A. (1981) Long-term carcinogenicity and toxicity studies of patulin in the rat. *J Appl Toxicol 1*, 256-61.
(85) Babish, J. G., Stoewsand, G. S., Furr, A. K., Parkinson, T. F., Bache, C. A., Gutenmann, W. H., Wszolek, P. C., and Lisk, D. J. (1979) Elemental and polychlorinated biphenyl content of tissues and intestinal aryl hydrocarbon hydroxylase activity of guinea pigs fed cabbage grown on municipal sewage sludge. *J Agric Food Chem 27*, 399-402.
(86) Wedig, J. H., Wentworth, R. A., Gallo, M. A., Babish, J. G., and Henion, J. D. (1978) Disposition of zinc pyrithione in the rat. *Food Cosmet Toxicol 16*, 553-61.
(87) Stoewsand, G. S., Babish, J. B., and Wimberly, H. C. (1978) Inhibition of hepatic toxicities from polybrominated biphenyls and aflatoxin B in rats fed cauliflower. *J Environ Pathol Toxicol 2*, 399-406.
(88) Babish, J. G., Stoewsand, G. S., and Lisk, D. J. (1978) Effect of diet on the hepatotoxicity of polybrominated biphenyls (FireMaster PB-6). *Environ Health Perspect 23*, 133-7.
(89) Babish, J. G., and Stoewsand, G. S. (1978) Effect of dietary indole-3-carbinol on the induction of the mixed-function oxidases of rat tissue. *Food Cosmet Toxicol 16*, 151-5.

(90) Babish, J. G., and Stoewsand, G. S. (1977) Polybrominated biphenyls: inducers of hepatic microsomal enzymes and type A cytochrome P450 in the rat. *J Toxicol Environ Health 3*, 673-82.
(91) Babish, J. G., and Stoewsand, G. S. (1975) Hepatic microsomal enzyme induction in rats fed varietal cauliflower leaves. *J Nutr 105*, 1592-9.
(92) Babish, J. G., Gutenmann, W. H., and Stoewsand, G. S. (1975) Polybrominated biphenyls: tissue distribution and effect on hepatic microsomal enzymes in Japanese quail. *J Agric Food Chem 23*, 879-82.

Book Chapters

Ma, X. and Babish, J.G. Activation of Signal Transduction Pathways by Dioxins. Chapter 29 in Molecular Biology of the Toxic Response. 1999, ed A, Puga and K.B. Wallace. Taylor & Francsis. Philadelphia, PA.

Patents (Twenty-one US and three foreign patents)

US Patent No. **7,332,185**	2/19/2008 Complex mixtures exhibiting selective inhibition of cyclooxygenase-2
US Patent No. **7,279,185**	10/9/2007 Curcuminoid compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2
US Patent No. **7,270,835**	9/18/2007 Compositions that treat or inhibit pathological conditions associated with inflammatory response
US Patent No. **7,205,151**	4/17/2007 Complex mixtures exhibiting selective inhibition of cyclooxygenase-2
US Patent No. **7,195,785**	3/27/2007 Complex mixtures exhibiting selective inhibition of cyclooxygenase-2
US Patent No. **6,979,470**	12/27/2005 Curcuminoid compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2
US Patent No. **6,908,630**	6/2120/05 Combinations of sesquiterpene lactones and ditepene triepoxide lactones for synergistic inhibition of cyclooxygenase-2
US Patent No. **6,780,596**	8/24/2004 Methods for determining the activity of complex mixtures
US Patent No. **6,733,793**	5/11/2004 Oral composition with insulin-like activities and methods of use
US Patent No. **6,629,835**	11/7/2003 Combinations of diterpene triepoxide lactones and ditepene lactones or triterpenes for synergistic inhibition of cyclooxygenase-2
US Patent No. **6,506,420**	1/14/2003 Combinations of psyllium and chitosan for synergistic adsorption of triglyceride
US Patent No. **6,140,063**	10/31/2000 In vitro screening assay for identification of compounds that inhibit cytopathicity of viral infection
US Patent No. **5,833,994**	11/10/1998 Use of the Ah receptor and Ah receptor ligands to treat or prevent cytopathicity of viral infection.
US Patent No. **5,612,188**	3/18/1997 Automated, multicompartmental cell culture system.
US Patent No. **5,529,899**	6/25/1996 Immunoassay for Ah receptor transformed by dioxin-like compounds.
US Patent No. **5,496,703**	3/5/1996 Indirect immunoassay for dioxin-like compounds
US Patent No. **5,057,510**	10/15/1991 Use of selected pyridine-2-thione-N-oxide compounds as growth promoters for poultry
US Patent No. **4,610,993**	9/9/1986 Use of selected pyridine-N-oxide disulfide compounds to treat or prevent bovine mastitis
US Patent No. **4,609,665**	9/2/1986 Use of selected pyridine-N-oxide disulfide compounds to treat or prevent swine exudative epidermitis
US Patent No. **4,401,666**	9/30/1983 Use of metallic salts of pyridine-2-thione-N-oxide to treat or prevent bovine mastitis
US Patent No. **4,401,666**	8/16/1983 Use of metallic salts of pyridine-2-thione-N-oxide to treat or prevent swine exudative epidermitis

185 Current US and Foreign Patent Applications

Dr. Cedric J. Pearce

Career summary

Scientifically-trained (microbial biochemistry and fermentation products) entrepreneur with twenty five years technical and management experience in academic and commercial biotech and pharmaceutical industry, including five years as a pharmacy professor (University of Connecticut), seven years in major pharmaceutical companies (Bristol-Myers, American Cyanamid), ten years in biotechnology industry including start-ups; sabbatical year working in the venture capital world, five years consulting to pharmaceutical and biotechnology companies. Founded two fermentation-based companies.

Work Experience in the Pharmaceutical and Biotechnology Industry

2000- 2008. Numerous advisory roles within the pharmaceutical and biotechnology industry; customers have included OSI Pharmaceuticals, Fournier (France), Japan Bioindustries Association (Tokyo), National Institutes of Health, InterLink Biotechnologies, Novobiotics, CiVentiChem, ASA Pharm (Ireland), A.M.Pappas and Associates.

2006 **Founded MycoFuels, Inc.** a biofuels company addressing issues around converting biomass into simple organic compounds using microbial approaches.

- Start up CEO

2001 **Founded Mycosynthetix, Inc**. a fungal metabolites research and microbiology service company.

- September 2001 – present **CEO** of Mycosynthetix, Inc.
- Involved in every aspect of starting and running the company including
  - Scientific direction
  - Hiring and training staff
  - Funding
  - Business development
  - Negotiating deals and contracts, including license deal with Dow AgroSciences potentially worth $20+mm over the term of the agreement.
  - Business contacts in industry and academia throughout the US, Asia especially Japan, and all major European countries
  - 2008 Directed selecting and up-fitting new business site in North Carolina – moved in May 2008 and opened for business in June

2004 – 2005 **Director of Business Development US and Canada,** Biofrontera AG, a German biotechnology company, Leverkusen and Heidelberg.

- Identified and pursued business opportunities for Biofrontera's discovery and pharmaceutical divisions

2000- 2001. **Vice President, Discovery Technologies**, A. M. Pappas and Associates,

Durham, NC.

- Acted as consultant to a number of pharmaceutical and biotechnology companies
- Assisted the venture capital side of the business with all aspects of business plan evaluation (the Company focused on pharmaceutical and biotechnology opportunities)
- Business development for consulting and investment opportunities
- Continued as an Associate (2005) and Limited Partner of the Company (current)

2000 –2003. **Vice President for Business Development and Natural Products Chemistry, Consultant and Member of the Scientific Advisory Board** for Interlink Biotechnologies, CA and NJ.

- Provided advisory services
- Managed the establishment of an organic chemistry research laboratory.

2000- 2001. **Director of MYCOsearch** and **Senior Advisor Natural Products Discovery,** OSI Pharmaceuticals, Durham NC.

- Supervised operational and fiscal needs of MYCOsearch.
- Managed all mycology and natural products chemistry, including consultants.
- Direct all fermentation work for in-house and collaborative projects
- Contribute to all programs involving natural products
- Advise on the natural products discovery programs within OSIP and act as company-wide expert on natural products and their use in the pharmaceutical environment
- Steering committee member for anti-viral discovery project
- Report to Executive Vice President, Drug Discovery, OSIP headquarters, Uniondale.

1998-2000. **Director of Natural Products Discovery**, MYCOsearch a subsidiary of OSI Pharmaceuticals, Durham NC.

- Direct the natural products discovery programs within OSIP
- Oversee operational and fiscal needs for the North Carolina operations of OSI Pharmaceuticals at MYCOsearch.
- Manage up to approximately 20 direct reports, including Ph.D. level scientists.
- Team building, including identifying, hiring and training of personnel.
- Natural product research direction, including setting strategies and priorities.
- Day to day involvement with research workers.
- Drug discovery project management in various areas, including antibacterial, antifungal and antiviral.
- Supervised anti-infective and cancer screening and evaluation of antibacterial compounds in *in vivo* infection models
- Company expert on natural products and their use in the pharmaceutical environment.
- Identifying innovative opportunities within the natural products/drug discovery area.
- Report to Executive Vice President, Drug Development, OSIP headquarters, Uniondale.

1996-1998. **Director, Microbiology (formerly Director Microbial Fermentation**), MYCOsearch a subsidiary of OSI Pharmaceuticals.

- Directed eight research scientists/technicians. Reported directly to VP, Pharmaceutical Operations.
- Had overall responsibility for all fermentation work. Supervised high throughput oriented fermentations and processing, involving the use of robots, and scale-up work to provide isolation groups with material for chemistry and pharmacology.
- Conducted research on individual lead cultures producing bioactive components and on methods development as and when needed.
- Coordinated fermentation supply to screening groups, involved in prioritization of leads for further work, help promote natural products research within the company and to help overcome technical issues associated with screening these materials for bioactivity.
- Initiated antibacterial discovery program including identifying unmet clinical needs, suitable targets and screening strategies. Coordinated/supervised internationally known consultants. Managed in-house screening endeavors, from assay screen development, through HTS, lead identification, and lead evaluation. Designed *in vitro* and *in vivo* systems for progression of suitable candidates.
- Continued involvement in strategic planning for OSIP's anti-infective discovery programs.

1994-1996. **Director of Microbiology/Fermentation**, MYCOsearch, Inc., Durham, NC.

- Directed the activities of six technicians.
- Maintained duties listed above, as well as visited labs of clients and potential clients to consult on discovering leads from fermentation sources, and to coordinate activity.
- Performed other functions associated with working for a small company, including visiting major pharmaceutical companies engaged in screening and helping to develop collaborations, as well as being involved in running and developing MYCOsearch as a business.

1989-1994. **Fermentation Group Leader**, Microbiology and Automated Technology Department, Natural Products Research Section (formerly Microbial Physiology Department, Infectious Diseases and Molecular Biology Research Section), Medical Research Division, Lederle Laboratories, American Cyanamid Company, Pearl River, New York.

- This was the main groups for antibacterial discovery within the Company; our role was to identify new targets, devise screening strategies, screen material for bioactivity, evaluate and prioritize leads, and provide material for in vivo testing.
- Supervised a group, consisting of up to three Ph.D. level and six technicians, whose role was to ferment all types of terrestrial and marine microorganisms including fungi and bacteria for the production of novel bioactive compounds for medical and agricultural uses, and to carry out screening for a variety of activities. Involved in scale-up fermentation using flasks and fermenters, optimization studies, and biotransformation/biosynthesis and directed fermentations.

- Served as one of six members of agricultural natural products discovery steering committee which assisted in focusing groups to find novel leads, and introduced agricultural screens to my group and directed their implementation.
- Interacted closely with chemistry to facilitate discovery of novel compounds.
- Participated in the prioritization of lead compounds for agricultural and medical use.
- Produced company reports on significant findings.

1988- 1989. **Senior Research Biochemist**, Microbial Physiology Department, Infectious Diseases and Molecular Biology Research Section, Medical Research Division, Lederle Laboratories, American Cyanamid Company, Pearl River, New York.

- Performed bench work and supervised two technicians engaged in biosynthesis and biotransformation reactions, and fermentation optimization,. Employed a variety of methods, with emphasis on HPLC and the use of stable isotopic labeling and mass spec/NMR. Instrumental in setting up lab, selecting and purchasing equipment, including HPLCs and radio-analytical apparatus.

June -August 1987 and June- August 1988. **Visiting Scientist**, Bristol-Myers Pharmaceutical Research and Development Division, Wallingford, CT.

- Conducted research on fermentations and biosynthesis of lead anticancer compounds.

<u>Academic and Teaching Experience</u>

2006-2007. **Tokubetsu Kenkyuin** (Visiting Professor), Tamagawa Academy, Tokyo, Japan.

2005-2007. **Visiting professor rôle** at North Carolina State University, Microbiology Department. Taught classes in biotechnology of microbial-derived pharmaceuticals and a course on entrepreneurship to MS students.

September 1983 -November 1988. **Assistant Professor in the Medicinal Chemistry and Pharmacognosy** Section, School of Pharmacy, The University of Connecticut, Storrs, CT.

- Taught natural products chemistry and biochemistry to pharmacy students; organized and managed labs; wrote grant applications and supervised research students.
- Conducted research in the areas of chemistry of antibiotics and anticancer fermentation products, biosynthesis and biotransformation of compounds, and antibiotic resistance.
- Collaborated with the NCI on fungal fermentations for anticancer/AIDS drug discovery.
- Served on the usual academic committees within the university.

January 1986 - December 1986. **Adjunct Assistant Professor in Molecular and Cellular Biology**, University of Connecticut, Storrs, CT.

- Taught pharmaceutically-oriented biotechnology to graduate students.

July 1980 - August 1983. **Radiochemist**, Radioisotope Laboratory, University of Illinois, Urbana, IL.

- Taught graduate course on the synthesis and use of isotopically-labeled compounds.
- Supervised and directed the University's radio isotope laboratory, taught research students techniques for synthesis and analysis of isotopically-labeled compounds, and collaborated with research groups involved in a variety of chemical/biochemical projects.

University Education

Department of Physiology and Biochemistry, The University of Southampton, England, B.Sc. (Hons).

Department of Physiology and Biochemistry, The University of Southampton, England, Ph.D. Thesis: "Studies on the Biosynthesis of Neomycins," supervised by Professor M. Akhtar and Dr. J.E.G. Barnett.

Postdoctoral Experience

Junior Teaching Fellow, Department of Physiology and Biochemistry, The University of Southampton, England. Taught biochemistry to medical students.

Royal Society European Exchange Fellowship, Institut de Chimie des Substance Naturelles, Centre National de la Recherche Scientifique, 91190 Gif sur Yvette, France. Dr. S.D. Gero. Mutasynthesis and biosynthesis of antibiotics.

Research Associate, School of Chemical Sciences, University of Illinois, Urbana. Professor K.L. Rinehart, Jr. Biosynthesis of antibiotics.

Specific Scientific Research Interests

- Microbial and fungal metabolites especially those used for infectious diseases, cancer and agricultural applications.
- New approaches to metabolite identification including high throughput methods.
- Infectious diseases and the study of antibiotics including the discovery of novel compounds, and resistance mechanisms.
- Bioassay and screening methods.
- The biosynthesis of microbial products and the application of biosynthetic principles to producing novel compounds.
- Biofuels and the conversion of biomass using microbial approaches.

Awards

- Royal Society European Exchange Fellowship, 1977
- Arnold O. Beckman Research Award, University of Illinois, October 1982.

- American Society of Pharmacognosy. Faculty travel grant to attend International Research Congress on Natural Products, Chapel Hill, NC, 1985.
- American Society of Biological Chemists, travel grant to attend 13th International Congress of Biochemistry, Amsterdam, 1985.

Articles Published

N. M. Irvine, C. N. Yerkes, P. R. Graupner, R. E. Roberts, D. R. Hahn, C. Pearce and B. C. Gerwick. Synthesis and Characterization of Synthetic Analogs of Cinnacidin, a Novel Phytotoxin from *Nectria* sp. 2007. Pest Management Science. In press.

G. T. Carter, J. B. Gloer, J. Kobayashi and C. Pearce; Special Issue in Honor of Professor Kenneth L. Rinehart. J. Nat. Prod. 70, 329-331. (2007).

P. Lewer, P. Graupner, D. Hahn, L. Karr, D. Duebelbeis, J. Lira, P. Anzeveno, S. Fields, J. Gilbert and C. Pearce. Discovery, Synthesis and Insecticidal Activity of a Novel Cycloaspeptide. J Nat. Prod. 69(10):1506-10 (2006).

C. Boros, C. Smith, Y. Vasina, Y. Che, A. Dix, B. Darveaux, and C. Pearce. Isolation and Identification of the Icosalides—Cyclic Peptolides with Selective Antibiotic and Cytotoxic Activities. J Antibiotics 59, 486-494 (2006).

J. D. Haley, D. E. Smith, J. Schwedes, R. Brennan, C. Pearce, C. Moore, F. Wang, F. Petti, F. Grosveld, S. M. Jane, C. T. Noguchi, and A. N. Schechter. Identification and characterization of mechanistically distinct inducers of γ-globin transcription. Biochem. Pharmacol. 66, 1755-1768 (2003)

C. Boros, A. Dix, B. Katz, Y.Vasina and C. Pearce. Isolation and identification of cissetin - a setin-like antibiotic with a novel cis-octalin ring fusion. J. Antibiotics 56, 862-865 (2003).

C. Boros, B. Katz, S. Mitchell, C. Pearce, K. Swinbank and D. Taylor. Emmyguyacins A and B: Glycolipids from a Sterile Fungus Species that Inhibit the Low pH Conformational Change of Hemagglutinin A during Replication of Influenza Virus. J. Nat. Prod. 65, 108-114 (2002)

P. Cai, D. Smith, B. Cunningham, S. Brown-Shimer, B. Katz, C. Pearce, D. Venables and D. Houck. 8-Methyl-Pyridoxatin: A Novel N-Hydroxy Pyridone From Fungus OS-F61800 that Induces Erythropoetin in Human Cells. J. Nat. Prod. 6, 397-399. (1999).

P. Cai, D. Smith, A. T. Mcphail, E. Krainer, B. Katz, C. Pearce, C. Boros, B. Caceres and D. Houck. Mycoepoxydiene Represents a Novel Class of Fungal Metabolites. Tetrahedron. Letters. 40 (1999) 1479-1482.

D. Abbanat, M. Leighton, W. Maiese, C. Pearce, E. B. G. Jones and M. Greenstein. Cell Wall-Active Antifungal Compounds Produced by the Marine Fungus *Hypoxylon*

oceanicum LL-15G256. I. Taxonomy and Fermentation. J. Antibiotics 51. 296-302 (1998).

A. Heguy, P. Cai, P. Meyn, D. Houck, S. Russo, R. Michitsch, C. Pearce, B. Katz, G. Bringmann, D. Feineis, D. L. Taylor and A. S. Tyms. Isolation and characterization of the fungal metabolite 3-O-methylviridicatin as an inhibitor of tumor necrosis factor alpha-induced human immunodeficiency virus replication. Antiviral Chemistry and Chemotherapy 9:149-155. 1998.

P. Cai, D. Smith, B. Katz, C. Pearce, D. Venables and D. Houck. Destruxin-A4 Chlorohydrin, a Novel Destruxin from Fungus OS-F68576: Isolation, Structure Determination, and Biological Activity as an Inducer of Erythropoietin. J. Nat. Prod. 61, 290-293. 1998.

P. Cai, D. Smith, B. Cunningham, S. Brown-Shimer, B. Katz, C. Pearce, D. Venables and D. Houck. Epolones: Novel Sesquiterpene-Tropolones from Fungus OS-F69284 that Induce Erythropoietin in Human Cells. J. Nat. Prod. 61, 791-795. 1998.

C. Pearce. Bioactive Fungal Metabolites. Advances in Applied Microbiology. 44. 1-85. 1997. Academic Press, NY, NY.

Cedric J. Pearce, Robert R. West and G. T. Carter. The Effect of Sinefungin on the Biosynthesis of Ganefromycin. Structures of Ganefromycins Delta 1-4. Tetrahedron Letters 36, 1809-1812 (1995).

G. Schlingmann, L. Milne, C. J. Pearce, D. B. Borders, M. Greenstein, W. M. Maiese and G. T. Carter. Isolation, Characterization and Structure of a New Allenic Polyine Antibiotic Produced by Fungus LL-07F275. J. Antibiotics 48, 375-379(1995).

C. Pearce. Discovering Novel Bioactive Compounds from Fungi. In Natural Products: Rapid Utilization of Sources for Drug Discovery and Development. Biomedical Library Services. 1995. pp1.72-1.94.

D. A. Steinberg, V. S. Bernan, D. A. Montenegro, D. R. Abbanat, C. J. Pearce, J. D. Korshalla, N. V. Jacobus, P. J. Petersen, M. J. Mroczenski-Wildey, W. M. Maiese and M. Greenstein. Glycothiohexides, Novel Antibiotics Produced by Sebekia sp LL-14E605. I. Taxonomy, Fermentation and Biological Evaluation. J. Antibiotics 47, 887-893 (1994).

V. S. Bernan, D. A. Montenegro, J. J. Goodman, M. R. Alluri, G. T. Carter, D. R. Abbanat, C. J. Pearce, W. M. Maiese and M. Greenstein. Martinomycin, a New Polyether Antibiotic Produced by *Streptomyces salvialis*. I. Taxonomy, Fermentation and Biological Activity. J. Antibiotics 47, 1434-1438 (1994).

G. Schlingmann, R. R. West, L. Milne, C. J. Pearce and G. T. Carter. Diepoxins, Novel Fungal Metabolites with Antibiotic Activity. Tetrahedron Letters 34, 7225-7228 (1993).

G. T. Carter, D. B. Borders, J. J. Goodman, J. Ashcroft, M. Greenstein, W. M. Maiese

and C. J. Pearce. Biosynthetic Origins of the Polycyclic Antibiotic, Citreamicin. J. Chem. Soc. Perkin Trans. 1. 1991, 2215-2219.

C. J. Pearce, G. T. Carter, J. A. Nietsche, D. B. Borders, M. Greenstein and W. M. Maiese. The Effect of Methylation Inhibitors on Citreamicin Biosynthesis in *Micromonospora citrea*. J. Antibiotics 44, 1247-1251 (1991).

K. S. Lam, S. Forenza, T. W. Doyle and C. J. Pearce. Identification of Indolepyruvic Acid as an Intermediate of Rebeccamycin Biosynthesis. J. Indust. Microbiol. 6, 291-294 (1990)

K. S. Lam, S. Forenza, T. W. Doyle and C. J. Pearce. Biosynthesis of Rebeccamycin, A Novel Antitumor Agent. Topics in Industrial Microbiology: Novel Microbial Products for Medicine and Agriculture (1989).

C.J. Pearce, T.W. Doyle, S. Forenza, K.S. Lam and D. Shroeder. The Biosynthetic Origins of Rebeccamycin. J. Nat. Prod. 51, 937-940 (1988).

C.J. Pearce. Antibiotics. in McGraw-Hill 1985 Yearbook of Science and Technology. pp. 81-83.

K. L. Rinehart Jr., J-R. Fang, W-Z. Jin, C.J. Pearce, K-I. Tadano and T. Toyokuni. Biotransformations and Biosynthesis of Aminocyclitol Antibiotics. Dev. Ind. Microbiol. 1985. 26:117-128.

J.-R. Fang, C.J. Pearce, and K.L. Rinehart, Jr. Neamine as an Intermediate for Neomycin Biosynthesis in *Streptomyces fradiae*. J. Antibiot. 37:77-79 (1984).

A.M. Jones, L.L. Melhado, T-H.D. Ho, C.J. Pearce and N.J. Leonard. Azido Auxins: Photoaffinity labeling of auxin-binding proteins in maze coleoptile with tritiated 5-azidoindole-3-acetic acid. Plant Physiol. (1984), 75:1111-16.

S.D. Gero, J. Cleophax, D. Mercier, M. Philippe, C.J. Pearce, B. Quiclet-Sire, D. Semeria and A.M. Sepulchre. Excursions into the field of aminocyclitol antibiotics: A bifurcated attack by fermentation and chemical approaches. In Chemistry and Biotechnology of Biologically Active Natural Products, Elsevier, Amsterdam (1984), pp. 79-112.

S. Hegde, R.M. Coates, and C.J. Pearce. The Preparation and Use of Lithium Triethylborotritide as a Tritium-labeling Reagent. Chem. Commun. (1983) 1484-85.

C.J. Pearce and K.L. Rinehart, Jr. The Use of Doubly-labeled 13C-Acetate in the Study of Streptolydigin Biosynthesis. J. Antibiot. 36, 1536-38 (1983).

L.L. Melhado, C.J. Pearce, M.M. d'Alarcao, and N.J. Leonard. Specifically Deuterated and Tritiated Auxins. Phytochemistry 21, 2879-2885 (1982).

K.L. Rinehart, Jr., M. Potgieter, W.-Z. Jin, C.J. Pearce, D.A. Wright, J.L. C. Wright, J.A. Walter, and A.G. McInnes. Biosynthetic Studies on Antibiotics Employing Stable Isotopes in Proceedings of the International Conference on Trends in Antibiotic Research. U. Umezawa, A.L. Demain, T. Hata, and C.R. Hutchinson, eds., Japan Antibiotics Research Association, Tokyo 141, Japan, 1982; pp 171-184.

C.J. Pearce and K.L. Rinehart, Jr. Aminocyclitol Antibiotic Biosynthesis in Antibiotics. Biosynthesis, Vol. IV. Springer-Verlag, Heidelberg, 1981. Edited by J. Corcoran.

C.J. Pearce, S. Ulrich, and K.L. Rinehart, Jr. Biosynthetic Incorporation of Propionate and Methionine into Streptolydigin. J. Am. Chem. Soc. 102, 2510-2512 (1980).

K.L. Rinehart, Jr., D.D. Weller, and C.J. Pearce. Recent Biosynthetic Studies on Antibiotics. J. Nat. Prod. 43, 1-20 (1980).

C.J. Pearce and K.L. Rinehart, Jr. Berninamycin Biosynthesis. 1. Origin of the Dehydroalanine Residues. J. Am Chem. Soc. 101, 5069-5070 (1979).

C.J. Pearce, M. Akhtar, J.E.G. Barnett, D. Mercier, A.-M. Sepulchre, and S.D. Gero. Sub-unit Assembly in the Biosynthesis of Neomycin. The Synthesis of 5-O-β-D-Ribofuranosyl and 4-O-β-D-Ribofuranosyl-2,6-dideoxystreptamines. J. Antibiot. 31, 74-81 (1978).

J. Cleophax, S.D. Gero, J. Leboul, M. Akhtar, J.E.G. Barnett, and C.J. Pearce. A Chiral Synthesis of D-(+)-2, 6-Dideoxystreptamine and Its Microbial Incorporation into Novel Antibiotics. J. Am. Chem. Soc. 98, 7110-12 (1976).

C.J. Pearce, M. Akhtar, C. Anthony, J.E.G. Barnett, and S.D. Gero. The Role of the Pseudo Disaccharide Neamine as an Intermediate in the Biosynthesis of Neomycin. Biochem. J. 159, 601-606 (1976).

A. Olesker, D. Mercier, S.D. Gero, C.J. Pearce, and J.E.G. Barnett. Confirmation of the Structure of myo-Inosamine Components of Minosaminomycin. Synthesis of Derivatives of D-myo-Inosamine-1. J. Antibiotics. 28, 490-91 (1975).

Patents Filed

P. Cai, D. Smith, D. Houck, B. Katz and C. Pearce. Natural Product Tropolones for Enhancing Biosynthesis of Erythropoietin, Composition Containing Same, and Method of Use. Filed November, 1996.

P. Cai, D. Smith, B. Katz and C. Pearce. Natural Product Benzopyran Compounds for Enhancing Biosynthesis of erythropoietin, Compositions Containing Same, and Method of Use. Filed November, 1996.

G. Schlingmann, L. Milne, C. J. Pearce, E. B. G. Jones and D. Albaugh. Novel

Fungicidal Agents LL-15G256 gamma, delta and epsilon Produced by LL-15G256 (Hypoxylon oceanicum). Filed June 2, 1995. Granted.

C. J. Pearce, G. T. Carter and R. R. West. Novel Metabolites by Methylation Inhibition. Filed 1994.

G. Schlinmann, R. R. West and C. J. Pearce. Isolation, Characterization and Structure of New Antibiotic Components Produced by Fungal Strain 07F275. Filed 1993.

Papers Presented at Meetings

Chang Hwa Hwang, Sang Hyun Cho, Cedric Pearce, and Scott G. Franzblau. High throughput screening of fungal cultures for anti tuberculosis activity. The 48th Annual Meeting of the American Society of Pharmacognosy, Portland, Maine. July 14-18th, 2007.

D. Tremblath, N. Oberlies, D. Kroll, C. Pearce, S. Khan and G. Riggins. Novel small molecule inhibitors of glioma cells expressing EGFRVIII. 15th International Congress of Neuropathology, San Francisco, California. September 9th-16th, 2006.

C. Boros, C. Smith,Y. Vasina,‡Y. Che, A. Dix, B. Darveaux, C. Pearce. Isolation and Identification of the Antibiotic Icosalide A1. The 47th Annual Meeting of the American Society of Pharmacognosy, Arlington, Virginia. August 5-9th, 2006.

J. Gilbert, P. Lewer, P. Graupner, D. Duebelbeis, E. Chapin, L. Karr, and C. Pearce. The Role of LC/MS in the Discovery of a Novel Insecticidal Cycloaspeptide. Presented at the 53rd American Society for Mass Spectrometry conference on mass spectrometry and related topics. San Antonio, Texas. June 5th-9th, 2005

P. Lewer, P. Graupner, J. Gilbert, L. Karr, E. Chapin, D. Duebelbeis, and C. Pearce. Isolation and identification of a novel insecticidal cycloaspeptide. P-248. Presented at the 46th Annual Meeting of the American Society of Pharmacognosy, University of Oregon. July 26-30, 2005.

*C.Pearce. Fungal Natural Products with Biological Activity. Meeting: Leverage Natural Products for Drug Development, Center for Business Intelligence. Philadelphia, February 2005.

*C.Pearce. Fungi: A Metabolite for Every Disease. Society for Industrial Microbiology, 55th Annual Meeting, Los Angeles, CA. August, 2004.

C. Pearce, B. Darveaux and C. Boros. Novel Fungal Metabolites. Society for Biomolecular Screening Annual Meeting, Madrid, Spain. October, 2003.

*C. Pearce. New Opportunities for Microbial Products in an International Market. 5th Workshop on Microbial Resources. Tamagawa University, Japan. June 2002.

*C. Pearce. Novel Biologically-active Fungal Metabolites. Society for Industrial Microbiology, 50th Annual Meeting. Arlington, VA. August 1-5, 1999.

*C. Pearce. Biologically-active Fungal Metabolites: Origins, Chemical Diversity and Pharmaceutical Activity. IBC 4th International Conference on Natural Products Drug Discovery and Development, Annapolis. June 15-16, 1998.

C. Pearce and B. Katz. The Dual Roles of Biodiversity and Fermentation Approaches in Generating Novel Fungal Metabolites. Presented at the 38th Annual Meeting of the American Society of Pharmacognosy, University of Iowa. July 26-30, 1997.

D. Houck, P. Cai, C. Pearce and B. Katz. Bioassay-Guided Isolation of EPO Induction Agents from Fungi OS-F3364. Presented at the 38th Annual Meeting of the American Society of Pharmacognosy, University of Iowa. July 26-30, 1997.

P. Cai, D. Houck, C. Pearce and B. Katz. Bioassay Guided Isolation of EPO Induction Agents from Fungi OS-F3666. Presented at the 38th Annual Meeting of the American Society of Pharmacognosy, University of Iowa. July 26-30, 1997.

C. Boros, B. Katz and C. Pearce. Isolation of Trichodermin using Assay for Inhibition of IL-2 Expression. Immunosuppressant activity of Trichothecenes. Presented at the 38th Annual Meeting of the American Society of Pharmacognosy, University of Iowa. July 26-30, 1997.

*C. Pearce. Pharmaceuticals and Biologically-Active Compounds Prodiuced by Fungi. New Approaches to Natural Products Drug Discovery. Profiting from Biodiversity in Combination with New Targets. NMHCC sponsored biotechnolgy conference, Baltimore November 12-14, 1997.

*C. J. Pearce. Bioactive Fungal Metabolites. Annual Meeting of the Society for Industrial Microbiology, Raleigh NC. August 1996.

*C. J. Pearce. Discovering Novel Bioactive Compounds from Fungi. International Business Communications conference on Natural Products: Rapid Utilization of Sources for Drug Discovery and Development. San Francisco, CA. May 1995.

*B. Katz and C. J. Pearce. High Throughput Screening for Drug Discovery, Cambridge Healthtech Institute. San Diego, CA. June 14-16, 1995.

*C. J. Pearce, B.Katz and C. Boros. Recent Advances in Bioactive Fungal Metabolite Discovery. International Summit on Drugs from Natural Products. Joint meeting of International Business Communications and China National Center for Biotechnology Development. Beijing, China. October 9-12, 1995.

*C. Pearce, B.Katz, P. Kulanthaivel, M. Chu, S. Singh and G. Schlingmann. Novel

Fungal Metabolites with Diverse Pharmaceutical Activities. Annual Meeting of the Society for Industrial Microbiology, Boston MA. July 1994.

*B. Katz and C. Pearce. Fungal Diversity and Fermentation Strategies for Successful Drug Discovery. IBC High Throughput Screening for Drug Discovery Meeting, San Francisco, CA. August 1994.

*B. Katz, C. Pearce, P. Kulanthaivel, M. Chu, S. Singh and G. Schlingmann. Novel Fungal Metabolites with Diverse Pharmaceutical Activities. Fifth International Mycological Conference. Vancouver, Canada. August, 1994.

M. Greenstein, G. Schlingmann, C. Pearce, G. Carter, L. Milne, P. Leighton, E. G. B. Jones and W. Maiese. Fermentation, Isolation and Identification of Antifungal Lactides from a Marine Fungus, *Hypoxylon oceanicum*. Fifth International Mycological Conference. Vancouver, Canada. August, 1994.

C. Pearce. The Role of Microorganisms in Drug Discovery. 10th NEMPET meeting, Blue Mountain Lake, NY June 1993.

C. Pearce, D. Roll, M. Lee, J. Manning, A. Fantini, J. Korshalla, D. Borders, M. Greenstein and W. Maiese. New LL-AO341 Antibiotic Components by Directed Biosynthesis with 5-Hydroxytryptophan. 34th Annual Meeting of the American Society of Pharmacognosy, San Diego, CA. July 1993.

D. A. Steinberg, V. S. Bernan, D. A. Montenegro, D. R. Abbanat, C. J. Pearce, J. D. Korshalla, N. V. Jacobus, P. J. Petersen, M. J. Mroczenski-Wildey, W. M. Maiese and M. Greenstein. Glycothiohexides. Novel Antibiotics Produced by *Sebekia* sp. LL-14E065: Taxonomy, Fermentation and Biological Evaluation. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA. October, 1993.

D. R. Abbanat, V. S. Bernan, D. A. Montenegro, D. A. Steinberg, C. J. Pearce, J. D. Korshalla, M. Alluri, G. T. Carter, W. M. Maiese and M. Greenstein. Pyrroindomycins, Novel Antibiotics Produced by *Kitasatosporia* sp. LL-42D005: Taxonomy and Fermentation. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA. October, 1993.

C. J. Pearce, B. Katz, J. D. Korshalla, N. V. Jacobus, P. J. Petersen, W. M. Maiese and M. Greenstein. Diepoxins, Novel Antibiotics from an Unusual Fungus LL-07F275: I. Taxonomy, Fermentation and Biological Activity. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA. October, 1993.

R. R. West, G. T. Carter, C. J. Pearce and D. B. Borders. Biosynthetic Studies on the Growth Promotant E19020. 32nd Annual Meeting of the American Society of Pharmacognosy, Chicago, IL. July, 1991.

A.. M. Reddy, G. T. Carter, C. J. Pearce and D. Borders. LC/MS Method for Qualitative

Analysis of Bafilomycins: A Comparison of Thermospray and Negative Ion CIMS. 31st American Society for Mass Spectrometry Conference, Tuscon, AZ. June, 1990.

C. J. Pearce, G. T. Carter, J. A. Nietsche, D. B. Borders, M. Greenstein and W. M. Maiese. The Effect of Methylation Inhibitors on Citreamicin Biosynthesis. 2nd International Conference on the Biotechnology of Microbial Products. Society for Industrial Microbiology, Sarasota, FL. October, 1990.

G. T. Carter, C. J Pearce, D. B. Borders, J. J. Goodman, J. Ashcroft, M. Greenstein, and W. M. Maiese. Biosynthesis of Citreamicin. 30th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta, GA. October, 1990.

K. S. Lam, S. Forenza and C. Pearce. Identification of Indolepyruvic Acid as an Intermediate of Rebeccamycin Biosynthesis. 89th Annual Meeting of the American Society of Microbiology. May, 1989.

K.S. Lam, S. Forenza, D.R. Schroeder, T.W. Doyle and C. Pearce. Biosynthesis of Rebeccamycin. The First International Conference on the Biotechnology of Microbial Products. Society for Industrial Microbiology, San Diego, CA. March 13-16, 1988.

M. Russell and C. Pearce. Mechanism of inactivation of chloramphenicol by chloramphenicol acetyl transferase. 28th Annual Meeting of the American Society of Pharmacognosy, University of Rhode Island, Kingston, RI. July 19-22, 1987.

K. L. Rinehart, D. D. Weller, C. Pearce, K. Tadano and K. M. Byrne. Biosynthetic studies on antibiotics. Twentieth meeting of the American Society of Pharmacognosy, Purdue University, IN, July 29-August 3rd, 19979.

***Invited speaker.**

Book Reviews

Pioneering Research; A Risk Worth Taking. J. Nat Prod. (2005)
Anthracycline Antibiotics. J. Nat. Prod. 59, 339 (1996).
Secondary-Metabolite Biosynthesis and Metabolism. J. Nat. Prod. 56, 2221 (1993).
Isotopes: Essential Chemistry and Applications. J. Nat. Prod. 44, 629 (1981).
Topics in Antibiotic Chemistry. J. Nat. Prod. 44, 629 (1981).

Scientific Committee Assignments

Chair, SBIR Special Review Panel, "Investigation pf the Production Parameters of Microbial Natural Products", NCI. 2006.
Ad hoc member of the Synthetic and Biological Chemistry study section B, NIH, 2005.
Member of American Society for Pharmacognosy Fellows Committee, 2004-6.
Member of the Organizing Committee for the 2003 American Society for Pharmacognosy Annual Meeting,

American Society of Pharmacognosy, Resolutions Committee Chair, 1997-2004.
Scientific Program Committee, 1994 International Forum on Advances in Screening Technologies and Data Management. 1993-1994.
American Cyanamid Company Agricultural and Medical Research Division Natural Products Program Review and Steering Committee, 1992-1994.
Lederle Science Lecture Series. Member 1989-1990. Chairperson 1991.
Biotechnology Education Committee, University of Connecticut, 1986-1988.
Scientific Program Committee for Annual Meeting of American Society of Pharmacognosy at the University of Rhode Island, 1986-87.
Fermentation Course Committee, University of Connecticut, 1985-1988.
NMR Committee, School of Pharmacy, University of Connecticut, 1984-89.
Biotechnology Steering Committee, University of Connecticut, 1984-1988.
Resolution Committee, American Society of Pharmacognosy, 1984-1990.
Fermentation and Separation Faculty Advisory Committee, Biotechnology Center, University of Connecticut, 1987 -1988.

History of Research Funding as Principal Investigator

- **Proposals Funded**

Subcontractor to Discovery of Anticancer Agents of Diverse Natural Origin, PI Prof Douglas Kinghorn, funded by the NCI for period 2007-2012

SBIR National Institutes of Health: Novel Broad and Narrow Spectrum Antibiotics Active against Bacteria 2004

National Cancer Institute. Fungal Fermentation, (contract no. NO1-CM-57692), $886,000 for period September 1985-September 1988

University of Connecticut Research Foundation .
Aminoglycoside biosynthesis and resistance, 1987
Antitumor antibiotic biosynthesis, 1985.
Antitumor antibiotic biosynthesis, 1985
Lyophilizer, 1985.
Biosynthesis of fortimicins, 1984.

Biomedical Research Support Grant (BRSG).
University of Connecticut
TLC Scanner, January 1986.
Fungal Metabolites, 1985.
The biochemistry of sorbistin production 1984.
The biosynthesis of fortimicins and related novel antibiotics. 1983.
University of Illinois
Liquid scintillation counter 1982.

Food and Drug Administration. Radiolabeled Neomycin B, contract no. 223-81-7068,

1981.

American Cancer Society. The biosynthesis of bestatins, 1984.

Arnold O. Beckman Research Award, University of Illinois. 1982.

- **Major Proposals Approved**

National Institutes of Health. The biosynthesis of acylaminoglycoside antibiotics.1987.
National Institutes of Health. The biosynthesis of gentamicins, 1985.
National Institutes of Health. Biosynthesis of biologically-active microbial products, 1984).
Food and Drug Administration. Biosynthetic labeling of streptomycin A and dihydrostreptomycin A with carbon 14. 1981.

Affiliations

Member of the American Chemical Society.
Member of the American Society of Pharmacognosy.
Member of the Society for Biomolecular Screening.
Member of the American Society for Microbiology.
Member of the Society for Industrial Microbiology.

References upon request