Research and innovation in the life sciences influences the development of new medicine, for example: studying the effects of the freeze-thaw cycle on the wood frog metabolism can help develop new ways of preserving human organs for transplant. Alternatively, researching chemistry, specifically the interactions between mitochondria, free radicals and antioxidants, and how they all affect aging in humans, can establish fundamental knowledge of which chemicals will help us reduce the effects of aging. Another example is how research in neuroscience enabled genetic engineers to increase/decrease the abilities of the mouse brain through DNA manipulation. Those are just some of the examples featured in this report of the various direct and indirect connections between life sciences and modern medicine.

Introduction

Life sciences include biology, medicine, anthropology, and ecology. Those branches of science deal with living organisms and their organization, life processes, and relationships to each other and their environment. “Life sciences” is also a general term for science programs in academia that are biologically-oriented – everything from the study of plants and animals to how they evolved and adapted over time to the molecular basis of life. The objective of this report is to examine how specific life sciences relate to medicine (biochemistry, chemistry, molecular biology and neuroscience. There is a concluding summary of the experimental models and techniques used by scientists working in various branches of life sciences, to reveal molecular mechanisms and their relevance to medicine.

Biochemistry – Cowan and Storey 2001

Wood frogs are known to freeze and survive when thawed. This paper examined the activity of enzymes, such as hexokinase, glucokinase and triosephosphate isomerse, in the major organs specifically the brain, heart, liver, kidney and muscles during freeze-thawing in wood frogs. Tissue samples were taken from the frogs that were placed in three separate groups; non-freezing conditions (5 degrees Celsius), freezing conditions (-3 degrees Celsius) and one under freezing and then normal conditions.
The major conclusion made based on the data, include that the freeze/thaw had affects on the amount of selected enzymes of intermediary metabolism of the frogs. The two reasons why a reduction in enzyme activity occurred in freeze-induced environments were: 1) the energy limitation resulting from ischemia would affect rates of ATP-dependent protein synthesis causing an imbalance in the synthesis versus degradation rates causing the net reduction in several enzymes in a frozen state. 2) Freeze induced changes in enzyme activity could represent changes in enzyme or pathway flux.

Understanding metabolic responses to physiological stresses (such as freezing) would aid in freezing organs for transplantation by storing them for longer periods of time.

Chemistry – Chepelev et al 2009

Evidence indicates that free radicals from mitochondria are a major contributor to cellular or biological aging. This paper deals with the effect of peroxyl radicals on the mitochondrial enzymes citrate synthase and aconitase as well as protection of citrate synthase from radical-induced damage by antioxidants such as naphthalenediols. Purified citrate synthase (CS) and isolated mitochondria were treated with AAPH.

The enzymatic activity was assayed using a microplate reader. Protein modifications were studied using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), Mass Spectrometry (MS), fluorescence activation and emission studies.

The results showed that CS was susceptible to oxidative modifications via AAPH though the radicals created only inactivated CS and had no effect on aconitase activity (meaning that CS can take some damage before enzyme inactivation occurs). CS is used as an index of mitochondria but can be damaged by reactive oxygen species (ROS). Because ROS are generated in many diseases this index may be unreliable. Antioxidants may aid in protecting the CS and other components of the cell from ROS and, perhaps, help people achieve healthier aging.

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The detailed knowledge of the molecular processes by which cells sense oxygen may be helpful in clinical interventions of conditions associated with hypoxia.

In mammalian cells, a lack of oxygen, or hypoxia, leads to the stabilization of a sequence-specific DNA binding transcription factor called HIF. This gene transcriptionally activates a variety of genes linked to processes such as angiogenesis and glucose metabolism. Drugs that stabilize HIF may augment angiogenesis and the adaptation to chronic hypoxia in animals and humans.

In this paper, the mechanism with which the tumor suppressor (HIF) protein binds to a transcription factor protein (pVHL, tumor suppressor gene in Von Hippel–Lindau (VHL) disease) was studied. This was done by changing amino acid coding regions of HIF gene by creating mutations for amino acids of interest (such as proline). Bound proteins were detected by immunoblotting and far western analyses techniques.

Peptides were analyzed by mass spectrometry to identify proline hydroxylation. These experiments resulted in identifying the nature of the modifications to the HIF gene. The results revealed that HIF undergoes hydroxylation at certain proline residues and that this is the mechanism for oxygen sensing at the transcriptional level. Drugs that stabilize HIF (transcription factor gene) may augment angiogenesis and the adaptation to chronic hypoxia in humans.

Toxicology – Padhi et al 2007

In the Canadian arctic, populations are exposed to multiple contaminants though there has been little to no research on how this affected the human population’s developing brains prior to this paper. In this project, rats were acquired, impregnated and then treated perinatally with the northern contaminant mixture (NCM), which represented the blood contamination level of the Canadian arctic population. This group was compared to those treated with the components of the NCM (methylmercury (MeHg), polychlorinated biphenyls (PCB) and organochlorine pesticides (OC)) separately and the control, propylthiouracil (PTU), which was administered in drinking water. The 14 cerebellum global gene of the litter born from the rats was observed for 14 days postnatally and the expression was measured.

It is interesting to note that the NCM had a lesser effect on the rats than that of MeHg, PCB and OC separately. Many differentially expressed genes from the components returned to control values in the NCM treated group. The scientists were also surprised by the magnitude of difference between the gender transcriptional responses to the contaminant exposure, suggesting that specific contaminants may pose gender-specific health risks. Human populations are continuously exposed to contaminants in the environment and food that affect our brain function. This study aided in our knowledge of neurotoxicity due to food toxins. This will help improve human health assessments of neurotoxicants and introduce preventative measures like changes in diet.

Figure 3. A model of pVHL[4].

Figure 4. A 3D model of methylmercury which is a common contaminant located in the Canadian arctic[5].
Neuroscience – Tsien 200

After exposure via the Late Show with David Letterman, this paper received a great deal of publicity due to the somewhat comedic idea of engineering mice with the capability to learn and memorize specific details greater than that of normal mice. Researchers were able to do this by “knocking out” the NR1 subunit of N-methyl-D-aspartate (NMDA) receptors in the hippocampus region of the brain, which created a mouse with poor spatial sense. Then they manipulated the NR2 subunit by adding more of it, Doogie mice were created (named after the television character Doogie Howser). These mice were able to distinguish between objects and recall specific locations that other mice could not. This was verified by an object-recognition test as well as the Morris water maze. The object-recognition test involved the mouse being placed with an object for five minutes and another for an additional five minutes. The mouse was then placed with one of the objects and a new object several days later, for another five-minute period. Doogie mice spent almost no time analyzing the old object and spent the time analyzing the new object, whereas other mice analyzed both[6].

The mice were also tested with the Morris water maze which involves a tank with specific symbols located on the walls and a clear platform located somewhere under the water. Using the symbols, Doogie mice were able to relocate the platform or look in the same quarter of the tank when the platform was removed. The results showed that genetic engineering could not create mice that are able to play Mozart’s pieces on the piano, but were able to create mice almost twice as smart as normal ones. Further study on the N-methyl-D-asparate (NMDA, brain receptor) could lead to the development of a drug that will increase activity of NMDA receptor, thereby improving memory of individuals with age-related memory disorders like Alzheimer’s disease.

Discussion

The relationship of some different branches of life sciences to medicine is depicted in Figure 6.

The previous synopsises of the selected peer-reviewed articles show the branches have many differences. These branches are very unique as they deal with specific topics such as biochemistry dealing with chemical processes in living organisms, chemistry, dealing with how organic and inorganic substances interact with one another, molecular biology, dealing with structure and function of macromolecules, toxicology, dealing with toxins, and neuroscience, dealing with the structure of the nervous system and brain.
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However, though they focus on different areas of study, the life sciences also have several similarities. An example is that many of the branches overlap with one another such as studying toxins that affect the nervous system (combination of toxicology and neuroscience\(^8\)) and studying the effect of substances on macromolecules within organisms (combination of chemistry, biochemistry and molecular biology\(^9,10\)).

The life sciences all assist in aiding the field of medicine. Biochemistry and chemistry study how certain chemicals can be used in humans to improve our quality of life. An example is adding chemicals to organs to freeze them for long periods of time so that they can be used without impairing integrity or functions. Molecular biology studies macromolecules, which may aid in understanding the human body and associated diagnoses of patients. Toxicology studies toxins and how to fight the toxins once they enter our bodies to reduce and eliminate negative effects. Neuroscience studies how to cure brain diseases and damage, to create a more inclusive society. Thus, life sciences play an essential role in medicine.

In terms of relatedness of different branches of life sciences to medicine, chemistry and molecular biology\(^9,10\) are the most distant from immediate application in human health because these studies need to be confirmed in animals first before also applying to humans. It takes about 10 years before a drug candidate (a small molecule) would become a drug because researchers start with experiments in a test tube (in vitro) and then move to test them in animals (in vivo).

Out of five papers discussed in this project, Tsien’s work\(^6\) is more closely related to a direct application in medicine as compared to the other four papers because that paper revolves around retrieving results that can have a direct relation to medicine. The other papers have an indirect relation.

Summary of the five articles selected from life sciences peer-reviewed literature.

Article 1:

Branch of Life Science: Biochemistry, Experimental Model: wood frog, Treatment: temperatures of -3°C and 5°C, Relevance to Medicine: understanding metabolic responses to physiological stresses such as freezing would aid in freezing organs for transplantation so organs can be stored for longer periods of time. Experimental Technique: The frogs were exposed to freeze and thaw cycles. The organs were recovered from treated frogs; enzymes were isolated and measured using a microplate reader.

Article 2:

Branch of Life Science: Chemistry, Experimental Model: Purified citrate synthase (CS) enzyme experiment, Treatment: Free radical generating compound (AAPH, 2,2’-azobis(2-amidinopropane) dihydrochloride,), Relevance to Medicine: CS is used as an index of mitochondria but can be damaged by reactive oxygen species (ROS). Because ROS are generated in many diseases this index is unreliable. Antioxidants aid in this as they assist in protecting the CS Experimental Technique: Purified CS and isolated mitochondria were treated with AAPH. The enzymatic activity was assayed using a microplate reader. Protein modifications were studied using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), Mass Spectrometry (MS), and fluorescence activation and emission studies.

Article 3:

Branch of Life Science: Molecular Biology Experimental Model: HIF peptide Treatment: Cobalt chloride, desferrioxamine. Relevance to Medicine: Tissue ischemia (oxygen starvation) is a major cause of morbidity and mortality via diseases such as mitral valve disease. Drugs that stabilize HIF (transcription factor gene) may augment angiogenesis and the adaptation to chronic hypoxia in humans. Experimental Technique: Bound proteins were detected by immunoblotting and far western analyses techniques. Peptides were analyzed by mass spectrometry to identify proline hydroxylation.
Article 4:
Branch of Life Science: Toxicology
Experimental Model: Rats
Treatment: Northern contaminant mixture, methylmercury, organochlorine pesticides, and polychlorinated biphenyls
Relevance to Medicine: Human populations are continuously exposed to contaminants in the environment and food that affect our brain function. This study aided in our knowledge of neurotoxicity due to food toxins. This will help improve risk assessments of neurotoxicants and introduce preventative measures such as changes in diet.
Experimental Technique: Rats were fed a contaminated diet. Total RNA was isolated, converted into cDNA and analyzed using Microarray Hybridization technique. Results of differential expression of RNAs were verified using real-time Quantitative PCR (qPCR) assay.

Article 5:
Branch of Life Science: Neuroscience
Experimental Model: Mice
Treatment: Knocking out specific genes and microinjections of additional NMDA subunits
Relevance to Medicine: Further study on the N-methyl-D-aspartate (NMDA, brain receptor) could lead to the development of a drug that will increase activity of NMDA receptor, thereby improving memory of individuals with age-related memory disorders such as Alzheimer’s Disease.
Experimental Technique: A subunit of NMDA receptor gene was inactivated using “knock-out” mice technology. Microinjection of normal NMDA receptor subunit gene was performed to increase the function of NMDA receptor in mice.