CHRONICLES OF MEDICAL HISTORY

BIOMIMETICS: THE EARLY YEARS

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ABSTRACT

Biomimetics is a relatively new term and an evolving discipline with the potentials for transforming every aspect of medicine. Biomimetics or biomimicry is the imitation of the models, systems, and elements of nature for the purpose of solving complex biological puzzles. Insights into biological processes have already resulted in new discoveries that are having immediate clinical applications. From the initial studies that were driven by anti-cancer objectives, biomimetics research has grown to include every aspect of biology and medicine. The early years (1974 – 1994) clearly showed an exponential rise in interest in this new discipline. This trend has continued unto the present. It is by mimicking nature that her immutable laws can be uncovered. Is the biomimetics approach man's tool for the ultimate conquest of sickness and disease? Only time will tell.

INTRODUCTION

Nigeria.

History has often predicted the direction of human activity. Science may be ranked as the human activity that has led to the most beneficial outcomes in all generations. Science is a system of organizing the knowledge about a particular subject; such knowledge as has been obtained by unbiased observation or experimentation in a reproducible and provable manner.

The sciences are classifiable into basic and applied. The basic sciences of physics, mathematics and chemistry often interact with the biological sciences. Advancements in biology are limited by precision of observation and variability of biological activities. The interphase between biology and the physical sciences accelerate developments in biological sciences. The impact of physical sciences in the subspecialty Radiology is undeniable. Human Medicine, an applied science with diverse sub-branches, is unarguably a very important stem of the biological sciences. Bioengineering, biotechnology, biophysics, biochemistry are a few of the disciplines that have resulted from interphases of physical and biological sciences.

The discovery of the structure of the DNA and eventually the illumination of the genetic code were outcomes of physical and biological interphases. This write up examines a potentially more significant discipline, Biomimetics. Biomimetics literally means imitations of life. The scope and the potential impact in human biology and medicine will be discussed and this historical review, based on the early publications on the subject as cited on PUBMED, will be a pointer to the future prospects of this new and emerging discipline.

History of Biomimetics

Historically, mankind has imitated models and elements of nature for the purpose of solving complex problems. The anatomy and flight of birds contributed to the discovery of human flying machines (aircrafts). Leonardo da Vinci (1425 - 1519) made numerous diagrams of flying machines from his close studies of bird flight. The Wright brothers who succeeded in devising aircrafts derived their ideas from observing birds, Otto Schmitt, an American physicist coined the term Biomimetics. His focus on devices that mimic natural systems led to the birth of the field of biophysics, and more recently, biomimetics.

Otto Herbert Schmitt (06 April, 1913 – 06 January, 1998)

Otto Herbert Schmitt was born at Missouri, USA. He attended Washington University, University of Minnesota, and University College, London. He was the third child of his parents. His extraordinary talent for invention started to show during his high school. His skill in the use of electrical instruments was developed very early in his educational journey. From high school he proceeded to the University of Washington on Sept 18, 1930 where he displayed unparallel skill in mathematics physics, and electronics. His graduate work was on the molecular organization of cells and tissues with special focus on nerve fibers. He utilized his prowess for electrical engineering to create artificial constructs that were able to mimic the formation and propagation of impulses along nerve fibers.

He earned his Ph.D with majors in physics and zoology. Within a short time after this he earned the National Research Fellowship of the United Kingdom which enabled him to do research on nerve impulses under Professor A.V. Hill, Nobel Prize winner and founder of biophysics at Woods Hole. It was during that time that Schmitt published a report on a novel bit of



Otto Herbert Schmitt

circuitry that won him fame. Prof Hill, recognizing Otto's talent, sought out additional sources of funding to keep Otto in London for as long as he could. Schmitt eventually had to return to the United States. He got a Faculty position at the University of Minnesota with a dual appointment to the departments of zoology and physics. University of Minnesota gave Otto incentives to keep him which included "Tenure as an associate professor (skipping the rank of assistant professor), a 28% pay rise, triple research funding, and guaranteed support for two graduate students." Otto had a natural flair for innovation and inventions. His work led to the formation of biophysics, biomedical engineering, and ultimately biomimetics. Biomimetics has grown as one of the largest areas of biomedical engineering, and this new discipline is rapidly expanding.

The Early Years of Biomimetics (1974 – 1994)

The early years of biomimtics as relevant to human medicine and clinical research could be seen by a PUBMED search of Biomimetics and Clinical Research. The search (done by this author on 22 December 2014) indicated that the early years of Biomimetics span from 1974 to 1994, a period of twenty years. Forty publications with the theme of biomimetics were published and listed on PUBMED. In 1974 Kupchan SM and Schubert RM published a paper titled 'selective alkylation: a biomimetic reaction of antileukemic triptolides.1' The reaction they described mimics the inhibition of tumor growth via selective alkylation of the thiol groups of key enzymes concerned with growth regulation. In 1978 Giannetti and others searched for new antibiotics from substances isolated from fruiting bodies of tremellous and *phlebia radiata*.² In 1979, Stevens MF and colleagues studied 'antitumor activities of biomimetic oxidation and metabolism of heterocyclic triazenes.3' In 1980 Le Quesne PW and his colleagues wrote on the 'Biomimetic synthesis of cathecol estrogens.⁴' In 1983, Dimmock JR and colleagues evaluated compounds that showed reactivity towards a biomimetic thiol.5 Finally, in 1983 kensler TW with two co-authors publish a report on 'inhibition of tumor promotion by a biomimetic superoxide dismutase.6' Their study suggested that reactive oxygen species played significant roles in the tumor promotion process. This paper ended the first set of clinically related biomimetic papers (the first ten years). These papers were mainly motivated by objectives of uncovering the secrets that may lead to cures for cancers.

The next ten years (1983 - 1994) returned 36 publications on the theme of biomimetics, an 85% increase. It was clear by that time that more and more researchers saw the young field as a very promising approach to discovery of underlying principles of biology. From cancer-related objectives, biomimetics research has rapidly grown to include other areas of medical investigation. The majority of the papers in this next era were on cancer-related biomimetics research, however, the other areas that were investigated included antibiotics, biosensor applications, ligandreceptor studies, metabolism, anti-parasitic agents (including evaluation of materials for anti-malarial activities), polymer chemistry (which led to nanosubstances), analytic chemistry, neurobiology, and medical imaging.⁷⁻⁴⁰ The growth of biomimetics has continued in an exponential rate with virtually every aspect of biology included. Perhaps the most fascinating aspect of biomimetics is biosensor research.

A biosensor is an analytical device, used for the detection of an analyte that combines a biological component with a physicochemical detector. The sensitive biological element could be any biological component e.g. a cell, tissue, organelle, cell receptor, enzyme, antibody, nucleic acid, etc. Biosensors utilize biomimetic processes to detect the analyte, generate amplifiable signals, which are further processed by a transducer (the physicochemical component). The physicochemical processes may be optical, electrical, electrochemical, etc. the resulting signals are amplified and recorded as quantifiable impulses in user-friendly

interphases. Automated biosensor systems have almost limitless applications.

Applications of biosensor systems are very diverse and universal, especially in biological disciplines. These include glucose monitoring, receptor-ligand interactions, metabolites detectors, all modalities of imaging, trace gas/element detectors, electronic thermometers, digital meters, microarrays, nanoscale biosensors, etc. The future of biomimetics research and applications will significantly be in the direction of biosensors as diagnostics and therapeutics.

CONCLUSIONS

Disease continues to plague mankind at unprecedented levels. Biomimetics research offers an innovative and different approach to our onslaught of pathogenic processes. For the first time in our history of science a discipline that sees the way nature sees has been born. It is obvious that biomimetics research has the potentials for transforming the way medicine is practiced. The results are as exciting as they are intriguing. We have started scratching at the surface of what nature has perfected over billions of years. It is by mimicking nature that her immutable laws can be uncovered in their purest forms. Is biomimetics man's tool for the ultimate conquest of sickness and disease? Only time will tell.

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REFERENCES

- 1. **Kupchan SM,** Schubert RM. Selective alkylation: a biomimetic reaction of the antileukemic triptolides? Science 1974;185(4153):791-3.
- Giannetti BM, Steglich W, Quack W, et al. [Antibiotics from basidiomycetes, VI. Merulinic acids A, B, and C, new antibiotics from Merulius tremellosus and Phlebia radiata (author's transl)]. Z Naturforsch C 1978;33(11-12):807-16.
- Stevens MF, Gescher A, Turnbull CP. Antitumour activity, biomimetic oxidation and metabolism of heteroalicyclic triazenes. Biochem Pharmacol 1979;28(6):769-76.
- 4. Le Quesne PW, Durga AV, Subramanyam V, *et al.* Biomimetic synthesis of catechol estrogens:

potentially mutagenic arene oxide intermediates in estrogen metabolism. J Med Chem 1980;23(3): 239-240.

- Dimmock JR, Shyam K, Hamon NW, et al. Evaluation of some Mannich bases derived from substituted acetophenones against P-388 lymphocytic leukemia and on respiration in isolated rat liver mitochondria. J Pharm Sci 1983;72(8):887-894.
- 6. **Kensler TW,** Bush DM, Kozumbo WJ. Inhibition of tumor promotion by a biomimetic superoxide dismutase. Science 1983;221(4605):75-77.
- 7. **Emery T,** Emery L, Olsen RK. Retrohydroxamate ferrichrome, a biomimetic analogue of ferrichrome. Biochem Biophys Res Commun 1984;119(3):1191-1197.
- 8. **Guzman F,** Cain M, Larscheid P, *et al.* Biomimetic approach to potential benzodiazepine receptor agonists and antagonists. J Med Chem 1984;27(5):564-570.
- 9. Egner PA, Kensler TW. Effects of a biomimetic superoxide dismutase on complete and multistage carcinogenesis in mouse skin. Carcinogenesis 1985;6(8):1167-1172.
- 10. **Maftouh M,** Besselievre R, Monsarrat B, *et al.* Synthesis and cytotoxic activity of hydroxylated derivatives of olivacine in relation with their biotransformation. J Med Chem 1985;28(6):708-714.
- 11. **Nakamura Y,** Colburn NH, Gindhart TD. Role of reactive oxygen in tumor promotion: implication of superoxide anion in promotion of neoplastic transformation in JB-6 cells by TPA. Carcinogenesis 1985;6(2):229-235.
- 12. **Trush MA,** Seed JL, Kensler TW. Oxidantdependent metabolic activation of polycyclic aromatic hydrocarbons by phorbol esterstimulated human polymorphonuclear leukocytes: possible link between inflammation and cancer. Proc Natl Acad Sci U S A 1985;82(15):5194-5198.
- 13. **Reiners JJ, Jr.,** Brott E, Sorenson JR. Inhibition of benzo[a]pyrene-dependent mutagenesis and cytochrome P-450 reductase activity by copper complexes. Carcinogenesis 1986;7(10):1729-1732.
- 14. **Tomoda R,** Kusunoki S, Nakashima K, Matsunaga T. Use of a copper-phthalocyanine membrane electrode for rapid preliminary detection of polycyclic mutagens. Mutat Res 1986;164(4):203-208.
- 15. **Dimmock JR,** Erciyas E, Kirkpatrick DL, King KM. Evaluation of some azines of aminomethylacetophenones and related quaternary ammonium compounds versus the EMT6 tumour. Pharmazie 1988;43(9):614-616.
- 16. Aiba S. Studies on chitosan: 2. Solution stability and reactivity of partially N-acetylated chitosan

derivatives in aqueous media. Int J Biol Macromol 1989;11(4):249-252.

- 17. **Hammel KE,** Tardone PJ, Moen MA, Price LA. Biomimetic oxidation of nonphenolic lignin models by Mn(III): new observations on the oxidizability of guaiacyl and syringyl substructures. Arch Biochem Biophys 1989;270(1):404-409.
- Shudo K, Hashimoto Y. [DNA modification and carcinogenesis—early events caused by a heterocyclic aromatic amine, Glu-P-1]. Gan To Kagaku Ryoho 1989;16(3 Pt 2):445-450.
- Burton SJ, Stead CV, Lowe CR. Design and applications of biomimetic anthraquinone dyes. III. Anthraquinone-immobilised C.I. reactive blue 2 analogues and their interaction with horse liver alcohol dehydrogenase and other adenine nucleotide-binding proteins. J Chromatogr 1990;508(1):109-125.
- 20. Feldman GM, Dannenberg AM, Jr., Seed JL. Physiologic oxygen tensions limit oxidant-mediated killing of schistosome eggs by inflammatory cells and isolated granulomas. J Leukoc Biol 1990;47(4):344-354.
- 21. Yamamoto S, Nakadate T, Aizu E, Kato R. Antitumor promoting action of phthalic acid monon-butyl ester cupric salt, a biomimetic superoxide dismutase. Carcinogenesis 1990;11(5):749-754.
- 22. **Duran HA,** de Rey BM. Differential oxidative stress induced by two different types of skin tumor promoters, benzoyl peroxide and 12-O-tetradecanoylphorbol-13-acetate. Carcinogenesis 1991;12(11):2047-2052.
- 23. **Shanzer A,** Libman J, Lytton SD, *et al.* Reversed siderophores act as antimalarial agents. Proc Natl Acad Sci U S A 1991;88(15):6585-6589.
- 24. **Bamford CH,** Al-Lamee KG. Chemical methods for improving the haemo-compatibility of synthetic polymers. Clin Mater 1992;10(4):243-61.
- 25. **Chen LX,** Lu JF, Wang K. The influence of bilirubin on fluidity and rotational correlation times of human erythrocyte membrane. Cell Biol Int Rep 1992;16(6):567-573.
- 26. **DeSesso JM,** Goeringer GC. Methotrexateinduced developmental toxicity in rabbits is ameliorated by 1-(p-tosyl)-3,4,4-trimethylimida zolidine, a functional analog for tetrahydrofolatemediated one-carbon transfer. Teratology 1992;45(3):271-283.
- 27. **Hoffman AS.** Present and emerging applications of polymeric biomaterials. Clin Mater 1992;11(1-4):13-18.
- 28. Lowe CR, Burton SJ, Burton NP, *et al.* Designer dyes: 'biomimetic' ligands for the purification of pharmaceutical proteins by affinity chromatography. Trends Biotechnol 1992;10(12): 442-448.

- 29. **Rueff J,** Rodrigues A, Laires A, Gaspar J. Activation of promutagens by porphyrinic biomimetic systems. Mutat Res 1992;269(2):243-250.
- Simske SJ, Luttges MW, Allen KA. Effect of oral calcium and calcium + fluoride treatments on mouse bone properties during suspension. Biomimetics 1992;1(4):311-327.
- 31. **Dillon CT,** Lay PA, Bonin AM, *et al.* In vitro DNA damage and mutations induced by a macrocyclic tetraamide chromium (V) complex: implications for the role of Cr(V) peptide complexes in chromium-induced cancers. Carcinogenesis 1993;14(9):1875-1880.
- Duran HA, Lanfranchi H, Palmieri MA, de Rey BM. Inhibition of benzoyl peroxide-induced tumor promotion and progression by copper (II) (3,5-diisopropylsalicylate) 2. Cancer Lett 1993;69(3):167-172.
- 33. **Ma Y,** Han GQ, Wang YY. [PAF antagonistic benzofuran neolignans from Piper kadsura]. Yao Xue Xue Bao 1993;28(5):370-373.
- 34. Nicot C, Vacher M, Denoroy L, et al. Limited proteolysis of myelin basic protein in a system mimetic of the myelin interlamellar aqueous space. J Neurochem 1993;60(4):1283-1291.
- 35. **Bulte JW,** Douglas T, Mann S, Frankel RB, Moskowitz BM, Brooks RA, *et al.* Magnetoferritin: characterization of a novel superparamagnetic MR contrast agent. J Magn Reson Imaging 1994;4(3):497-505.
- 36. **Hasmonay H,** Hochapfel A, Betrencourt C, *et al.* Lasalocid and biomimetic membranes: insertion in Langmuir films of lipids. Biochim Biophys Acta 1994;1193(2):287-292.
- Inbar J, Chet I. A newly isolated lectin from the plant pathogenic fungus Sclerotium rolfsii: purification, characterization and role in mycoparasitism. Microbiology 1994;140 (Pt 3):651-657.
- Krieg M, Bilitz JM, Srichai MB, Redmond RW. Effects of structural modifications on the photosensitizing properties of dialkylcarbocyanine dyes in homogeneous and heterogeneous solutions. Biochim Biophys Acta 1994;1199(2):149-156.
- 39. **Plant AL,** Gueguetchkeri M, Yap W. Supported phospholipid/alkanethiol biomimetic membranes: insulating properties. Biophys J 1994;67(3):1126-1133.
- 40. **Santambien P,** Sdiqui N, Hebert E, *et al.* [Studies of in vitro and in vivo toxicity of dyes used in affinity chromatography]. Ann Pharm Fr 1994;52(3):137-152.