

INTRODUCTION TO THE 31ST OLD HERBORN UNIVERSITY SEMINAR ON
EVOLUTIONARY BIOLOGY OF THE VIROME,
AND IMPACTS IN HUMAN HEALTH AND DISEASE
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***“A MATHEMATICAL PROBLEM SHOULD BE DIFFICULT IN ORDER TO
ENTICE US, YET NOT COMPLETELY INACCESSIBLE, LEST IT MOCK
AT OUR EFFORTS. IT SHOULD BE TO US A GUIDE POST ON THE
MAZY PATHS TO HIDDEN TRUTHS, AND ULTIMATELY A REMINDER
OF OUR PLEASURE IN THE SUCCESSFUL SOLUTION.”***

(David Hilbert, Paris, 1900)

Dr. Hilbert describes an important notion in science and that it is important to select an area where scientific endeavour is both rewarding and achievable. For the individual, selecting the right frontier in science is almost a matter of taste as it must consider selecting a topic that truly advance a field that are considered in the context of emerging theories, new techniques, and new ideas (*Greenwood, 1992*). Frontiers in science are everywhere.

Since 1987, the Old Herborn University Seminar has been exploring and celebrating the frontiers of science as they relate to the microbiome of the environment and living things. As with the individual embarking upon a career in a frontier in a particular science, the Old Herborn University Executive and Scientific Program Committees identified a topic which was ripe for consideration as the topic of a seminar, and that was the, “Evolutionary Biology of the Virome and Impacts on Human Health and Disease.” At first glance, one might question the consideration of this topic given the

relative infancy of our understanding of the virome relative to the vast amount of research that has been conducted on the bacteriome (Figure 1). Indeed, the field is considered in its infancy in understanding the structure, composition, and function of the bacteriome and interactions with human health and our ability to modify it to cure disease (*Marchesi, 2016*). Despite this fundamental challenge, the selection of the topic, which had not previously been considered by the OHUS, emerged from a number of important reasons. Firstly, the evidence to date recognizes the vast success of viruses in abundance (though not biomass) throughout the world. For example, viruses account for 94% of all nucleic acid containing entities in the oceans (*Suttle, 2007*), and the number of viral particles in the human gut roughly equates to the number of bacteria (*Kim, 2011*). To further imagine the power and potential of viruses in the world, Landenmark and colleagues estimated the quantity of DNA (of which viruses play a substantial contributor) in the biosphere as an estimate of the vast storage and

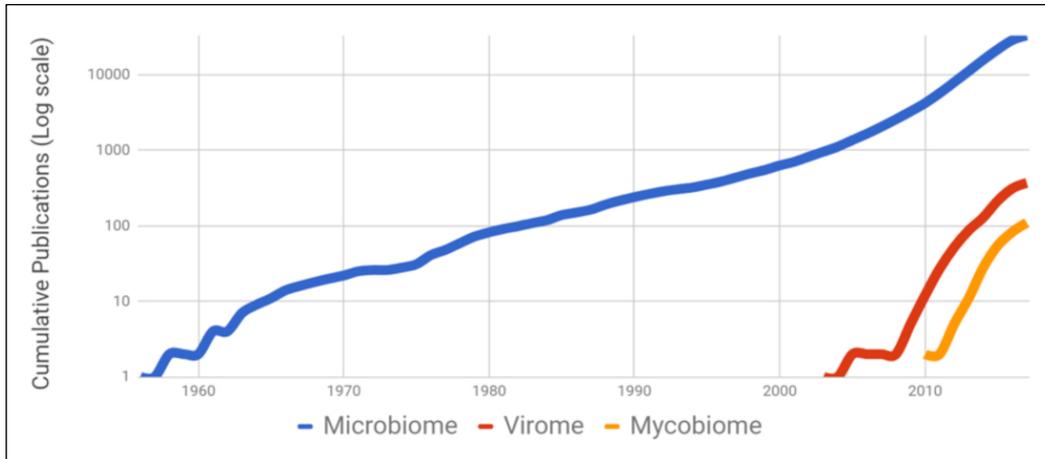


Figure 1: Relative force of publications related to phylum-specific research of the microbiome.

biological power that exists (*Landenmark, 2015*). The estimate that was generated was 5.3×10^{31} megabase pairs (Mb) which equates to 10^{21} computers with the mean storage capacity of the world's four most powerful supercomputers. To put this into further perspective, 10^{21} is the order of magnitude that is estimated to quantify the amount of grains of sand on the beaches of the world. To simply state, with viruses, big things come in small packages. With such vast "biological computational power", the virome is integral to our understanding of the world with applications to evolutionary biology, engineering, botany, synthetic biology, ecology, emerging infectious diseases, agriculture, aquaculture, and animal health (including humans) (*Parker, 2016*).

A second reason to consider the virome is the recognition that with viruses: *We are them, and they are us*. While commonly used as the context underlying many a scientific fiction novel and movie, it is estimated that at least 8% of human DNA is composed of retroviral genome, and over 100,000 known viral particles exist in human genome (*Horie, 2010*). And the impact of viruses on human evolution and suc-

cess is impressively highlighted by the discovery about two decades ago (*Mi, 2000*), where a gene in the human genome which encoded for a unique protein 'syncytin' made only by placental cells was discovered. Surprisingly, the gene appeared to be viral in origin and in its molecular characterization. A similar gene has also been identified in other primates, including chimpanzee placental cells. Subsequently, *Heidmann and colleagues (Dupressoir, 2005)* discovered a similar gene in other mammals including dogs, cats, pandas, hyenas and other carnivores. The syncytin gene appears to be strikingly similar in all species tested to date. It is noteworthy that syncytin is synthesized in the placental cells which are in direct contact with the uterine mucosal surface. Syncytin is responsible for the cell fusion and development of Syncytiotrophoblast. This cellular layer is essential for foetal survival and the transport of all soluble and cellular products from the maternal to the foetal circulation. It has been proposed that syncytin may have initially evolved to allow the virus to fuse host cells in order to facilitate cell-to-cell virus spread. Such a viral-induced process also allowed developing mam-

malian organisms to induce foetal cell fusion locally in the uterus to maternal cellular genome to facilitate maternal transport of nutrients and gasses essential for foetal survival. Thus, it has been said, “If not for a virus, none of us would ever be born.” (Zimmer, 2014)

While the individual scientist (and rather science teams in today’s world) approaches advancement through use of knowledge, honing of laboratory methods, and experimentation, the advancement that is intended from the OHUS is through what may be best termed consilience, or the ‘jumping together’ of knowledge by the linking of

facts and fact-based theory across disciplines (Wilson, 2000). Therefore, to address this formidable challenge, a diverse group of leading scientists across multiple disciplines of evolutionary biology, virology, bacteriology, computational biology, immunology and other domains were assembled to review emerging research across the spectrum of fundamentals of virome in single cellular organisms, the virome of multicellular organisms, and the interaction of virome on human health and disease. And a fruitful and productive endeavour it was.

LITERATURE

- Dupressoir, A., Marceau, G., Vernochet, C., Bénit, L., Kanellopoulos, C., Sapin, V., and Heidmann, T.: Syncytin-A and syncytin-B, two fusogenic placenta-specific murine envelope genes of retroviral origin conserved in Muridae. *Proc. Natl. Acad. Sci. USA.* 102, 725-730 (2005).
- Greenwood, A.: *Science at the frontier. Volume 1.* The National Academies Press, Washington, DC (1992).
- Horie, M., Honda, T., Suzuki, Y., Kobayashi, Y., Daito, T., Oshida, T., Ikuta, K., Jern, P., Gojobori, T., Coffin, J.M., and Tomonaga, K.: Endogenous non-retroviral RNA virus elements in mammalian genomes. *Nature* 463, 84-87 (2010).
- Kim, M.-S., Park, E.-J., Roh, S.W., and Bae, J.-W.: Diversity and abundance of single-stranded DNA viruses in human feces. *Appl. Environ. Microbiol.* 77, 8062–8070 (2011).
- Landenmark, H.K., Forgan, D.H., and Cockell, C.S.: An Estimate of the Total DNA in the Biosphere. *PLoS Biol.* 13, e1002168 (2015).
- Mi, S., Lee, X., Li, X., Veldman, G.M., Finnerty, H., Racie, L., LaVallie, E., Tang, X.Y., Edouard, P., Howes, S., Keith, J.C. Jr., and McCoy, J.M.: Syncytin is a captive retroviral envelope protein involved in human placental morphogenesis. *Nature* 403, 785-789 (2000).
- Marchesi, J.R., Adams, D.H., Fava, F., Hermes, G.D., Hirschfield, G.M., Hold, G., Quraishi, M.N., Kinross, J., Smidt, H., Tuohy, K.M., Thomas, L.V., Zoetendal, E.G., and Hart, A.: The gut microbiota and host health: a new clinical frontier. *Gut* 65, 330-339 (2016).
- Parker, M.T.: *An Ecological Framework of the Human Virome Provides Classification of Current Knowledge and Identifies Areas of Forthcoming Discovery.* *Yale J. Biol. Med.* 89, 339-351 (2016).
- Suttle, C.A.: Marine viruses--major players in the global ecosystem. *Nat. Rev. Microbiol.* 5, 801-812 (2007).
- Wilson, E.O.: *Consilience: The Unity of Knowledge.* Abacus, London (2010).
- Zimmer, C.: *A Planet of Viruses.* The University of Chicago Press, Chicago (2014).