Sex, Cancer and Evolution

- a sneak preview of a member's hot upcoming GENOME article -

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A common response when considering the biological meaning of sex is "isn't it obvious?" The typical biology textbook rejoinder is that biodiversity is the key evolutionary benefit of sexual reproduction, and that asexual reproduction is a less sophisticated "Xerox" copying process that does not produce the drastic changes needed to facilitate evolution. In the past 100 plus years, different approaches have been used within the framework of this type of thinking to produce evidence to support this seemingly obvious hypothesis. However, the paradox of sex is that sexual reproduction persists despite its overwhelming disadvantages.

A fresh viewpoint that challenges this "obvious" view comes from a chromosome guy turned cancer researcher, Henry Heng, who trained in the labs of Drs Lap Chee Tsui and Peter Moens, two prominent Society members who specialize in cutting edge molecular biology and meiosis research and evolution respectively.

Over the past eight years of research in his own lab at the Center for Molecular Medicine and Genetics, and the Karmanos Cancer Institute at Wayne State University, this somewhat unusual training led Henry to recognize the overwhelming genetic diversity of cancer both between patients with the same type of cancer as well as between cells of a single tumour of a individual - an observation that pointed to an Achiles' heel in the gene-centric approach to cancer research. While the importance of the gene in itself is undisputable, the relationship between genes and their higher level of organization defined by their chromosomal karyotype is what characterizes the genome. This organized system as a whole is now recognized as as the unit of evolution that plays a major role in both evolution and cancer initiation and progression. (See Genome, 49: 195-204, 2006; BioEssays, 2007).

Using the concept of genome aberration rather than gene mutation to re-examine the conceptual framework of the prevailing theories of cancer has provided some interesting developments. While cancer has long been considered a gene-based disease caused by a stepwise accumulation of some commonly shared gene mutations, this key assumption has be far from proven. Ever-accumulating data of mutation profiling generated from the large scale cancer genome sequencing paradoxically challenge this assumption. On the other hand, genome variation has been extensively linked to cancer. The analysis of chromosomes from individual cells during representative stages in cancer shows a correlation between patterns of chromosomal abnormalities and specific evolutionary stages. Two distinctive phases of evolution are evident: a relatively stable phase and an unstable phase of evolution with associated unpredictable random genome level changes. In this light, cancer progression is a non-linear process driven not by gene mutations but by genome variation-mediated cancer evolution (J Cell Physiology, 208: 461-472, 2006; J Cellular Biochemistry, 98: 1424-1435, 2006).

Consideration of cancer development from the 'above-gene' level has also led to insight on evolutionary issues such as sexual vs non-sexual reproduction. Heng's team has found a link between karyotypic evolution and system stability such as that found in cancer progression. During an unstable phase, karyotypes constantly evolve, displaying punctuated patterns of evolution; within a stable phase, stepwise evolution dominates. This brought into question some of the traditional thinking about sexual reproduction. In particular, the high level of genetic diversity should be linked with the sexual process and the genetic stability to the asexual process. If their cancer model was accurate and correctly reflected evolutionary principles, then two key assumptions needed to be re-examined, namely 1) asexual reproduction generates less genetic diversity; and 2) sexual reproduction generates high levels of genetic diversity.

Reexamination of previously reported evidence from this new perspective demonstrated that the two assumptions should be reversed. Similar to their new cancer framework, the answer lies at the genome level rather than at the gene level: sexual reproduction reinforces stability at the genome level by eliminating individuals with drastically altered karyotypes. Thus, sexual reproduction serves as a mechanism to "filter out" abnormalities within the species. So, while the traditional perspective shows sexual reproduction as an inefficient way to propagate, it is actually an effective way to preserve and perpetuate a species while still tolerating controlled diversity mainly at the gene and sub-chromosomal level.

Who would have known that there would be an intimacy between sex and cancer and that the connection would be evolution!

For additional reading on this subject see:
Heng HH, 2007. Elimination of altered karyotypes by sexual reproduction preserves species identity. Genome (in press).
Heng HH, 2007. Cancer genome sequencing: the challenges ahead. BioEssays (in press).
Ye et al, 2007. The dynamics of cancer chromosomes and genome. Cytogenetics and Genome Research (in press).

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