AUTHOR COMMENTARIES - From Special Topics

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Michael Skinner
From the Special Topic of Epigenetics

According to our Special Topics analysis on Epigenetics research over the past decade, the paper "Epigenetic transgenerational actions of endocrine disruptors and male fertility" (Anway MD, et al., Science *308[5727]: 1466-9, 3 June 2005) is a key paper in the Research Front Map on Epigenetic Gene Regulation. The paper, written by Dr. Michael Skinner and his team of research fellows at Washington State University, has 234 cites to its credit for the period ending October 31, 2008 in* Essential Science Indicators℠ *from Thomson Reuters.*

Dr. Skinner is a professor in the School of Molecular Biosciences at Washington State University. He also established two research centers there: the Washington State and University of Idaho Center for Reproductive Biology and the Center for Integrated Biotechnology. He served as the director of these centers for many years, but stepped down in 2008 to concentrate more on his own research efforts.

His record in our database includes 91 papers, the bulk of which are classified in Biology & Biochemistry, cited a total of 2,345 times.

This month, ScienceWatch.com *talks to Dr. Skinner about the paper and its impact on the field.*

SW: Would you please describe the significance of your paper and why it is highly cited?

In our paper, we were exploring whether exposure to environmental compounds such as endocrine disruptors (either the anti-androgenic fungicide vinclozolin or the estrogenic pesticide methoxychlor) during gestation in rats would result in decreased spermatogenic capacity and increased male infertility in the next generation. Although only the original generation mother was exposed to the compounds, we observed these effects in nearly all males of all the subsequent generations studied (up to four generations).

Subsequent studies have demonstrated effects on a wide variety of adult onset disease states. The idea that environmental factors could epigenetically reprogram the germ line in this fashion was a novel idea for how environmental factors may influence disease etiology. In essence, what your grandmother was exposed to when she was pregnant may cause disease in you and your grandchildren.

SW: How did you become involved in this research, and were there any particular successes or obstacles that stand out?

I did my B.S. in chemistry at Reed College in Portland, Oregon, my Ph.D. in

biochemistry at Washington State University, and my postdoc at the C.H. Best Institute at the University of Toronto. Prior to returning to Washington State as a professor, I was on the faculty of Vanderbilt University in Nashville, Tennessee, and the University of California, San Francisco.

My research focuses on exploring the manner in which different cell types in a tissue interact and communicate to regulate the growth and differentiation of gonads. We were investigating the effects of the environmental compounds on gonadal sex determination and serendipitously found these epigenetic transgenerational effects on adult onset disease.

"It will be important to determine what other disease states can come about through epigenetic effects of environmental factors."

SW: Where do you see your research and the broader field leading in the future?

The broader direction is determining the role of epigenetics in disease etiology and how environmental factors can promote adult onset disease and alter biological processes. Because the doses of the endocrine disruptors in our study were higher than levels occurring in the environment, we need to employ dose curves and toxicology studies to see if environmental levels also cause these transgenerational effects. We also need to test other compounds for their potential epigenetic transgenerational effects. The current focus is elucidating the molecular mechanisms involved in reprogramming the germ line and transgenerational nature of the phenomena. It will be important to determine what other disease states can come about through epigenetic effects of environmental factors.

SW: What are the implications of your work for this field?

These results have implications for toxicology, evolutionary biology, and the molecular basis of heritable disease. With regard to toxicology, we showed that the potential danger of environmental toxicants known as endocrine disruptors could have a long-lasting, transgenerational effects. Secondly, we also demonstrated that an environmental factor could trigger an epigenetic change to a genetic trait, which impacts our view of evolutionary biology. Thirdly, there were implications that events in embryonic and fetal development can affect disease states in adults. Epigenetics will be a critical process involved in how environmental factors influence biological processes and disease.

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Michael Skinner's current most-cited paper in *Essential Science Indicators*, with 234 cites:

Anway MD, *et al.*, "Epigenetic transgenerational actions of endocrine disrupters and male fertility," *Science* 308(5727): 1466-9, 3 June 2005. Source: *Essential Science Indicators* from Thomson Reuters.

Keywords: EPIGENETIC TRANSGENERATIONAL ACTIONS; MATERNAL CARE EFFECTS; EPIGENETIC GENE REGULATION; EPIGENETIC DIFFERENCES ARISE; EPIGENETIC PROGRAMMING.

PDF

back to top

Special Topics : Epigenetics : Michael Skinner Interview - Special Topic of Epigenetics

Scientific Home | About Scientific | Site Search | Site Map