

'From Promising to Predictive'

With Advances In Genomics, Exosomes Broaden Horizons

By Anette Breindl
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Exosomes – small vesicles that are shed from cells and contain circulating nucleic acids, or CNAs – have been known for some time to play a role in cell-to-cell communication in plants, Brian Durie told *BioWorld Today*. But in animals, they are still “an underappreciated biologic mechanism.”

But Durie, who is medical director of the International Myeloma Foundation, is working with researchers from the U.S./Germany firm Chronix Biomedical to harness that mechanism for both diagnosis and prognosis of disease. And recent publications showed that they may be a valuable tool in a diverse array of diseases, including both human and animal diseases.

Exosomes share some similarities to single-nucleotide polymorphisms (SNPs) in that both relate changes in DNA sequence to disease. But, Chronix CEO Howard Urnovitz told *BioWorld Today*, “one measures the past, and one measures the present. And we believe that measuring the present has enormous value to health care.”

Specifically, SNPs “really tell you about your past” – in the form of inherited risk factors – “and doing predictive modeling from them has been difficult.”

In contrast, he said, CNA signatures “can tell you about the present, and hopefully, the future,” by taking a snapshot of the DNA as it currently exists within the cells of the body.

Such snapshots consist of two parts, Urnovitz said. Genomic DNA that ends up in exosomes is part of normal cellular housekeeping, and “an active secretion of certain signature sequences” that can be used to both diagnose and predict disease.

Chronix plans to harness such signature sequences for a variety of diseases. The company is interested in cancer, and presented data at the 2008 American Society of Hematology meeting, which showed that in myeloma, CNA signatures can predict relapses before they become clinically apparent.

Urnovitz said that Chronix also is interested in applying the technology to breast, prostate and lung cancer. Researchers from Massachusetts General Hospital and Exosome Diagnostics Inc. also recently published data showing that exosomes also may be valuable as biomarkers to guide targeted therapy and monitor treatment response in glioblastoma. (See *BioWorld Today*, Dec. 29, 2008.)

For now, Chronix researchers are laying the groundwork for applications. The company, with collaborators from the German University of Goettingen, recently published an analysis of the circulating exosomes over time in apparently healthy human volunteers in the journal *Clinical Chemistry*.

“Apparently” is the operative phrase: In the course of their study, the scientists uncovered a hidden hepatitis B infection in one of their “healthy” volunteers. A similar event occurred in the myeloma patient described in the ASH abstract. Here, the scientists realized that a secondary cancer had developed in the myeloma patient, before it was clinically apparent.

The work published in *Clinical Chemistry* comes on the heels of a January publication in the journal *Nucleic Acids Research*. Here, the Chronix researchers published data showing that by monitoring the exosome signature in cattle and elk that were infected with transmissible spongiform encephalopathies, which cause mad cow disease in cattle and an equivalent disease in elk, they were able to detect a tell-tale infection signature months before any clinical symptoms were visible.

Chronix’ long-term plan is to develop databases of CNA signatures and partner with diagnostic firms to develop clinical tests that would be used to diagnose disease, and clinical labs for prognostic tests that would be used to guide treatment decisions.

Urnovitz acknowledged that, especially in the case of diagnosing novel diseases, “we are only as good as the databases that are out there.” But, he added, as such genomic databases grow by leaps and bounds, so do the prospects of the approach.

Genomics currently is often described as promising, he said, because much of it does not yet have the scientific rigor necessary for medical applications. But “we’ve turned it from promising to predictive.”