Emerging Company Profile

GeNeuro: Unraveling secrets of HERV

By Christopher Maggos
Senior Writer

GeNeuro S.A. thinks its work on human endogenous retroviruses may have uncovered the cause of neurodegenerative diseases like multiple sclerosis and as a result may offer a new therapeutic strategy. The company has an antibody against a HERV-W envelope protein in preclinical testing.

"Originally it was suspected that an HTLV — or human T-lymphotropic virus — was causing MS," CSO Herve Perron told BioCentury. "So when I found in 1989 a retrovirus in MS patients, it was not totally unexpected." The 1989 finding was published in *Research in Virology* and confirmed in a 1991 *Lancet* publication, also by Perron.

What was unexpected was the type of retrovirus he had discovered. "It belonged to a totally unstudied category of retroviruses," Perron said.

Much of Perron's work was done while he was at bioMérieux S.A. (Euronext:BIM, Marcy l'Etoile, France), which has since chosen to focus exclusively on diagnostics. Perron, BIM and Eclosion S.A., a Geneva seed fund, formed GeNeuro around the IP that Perron and BIM had developed for HERVs.

According to Perron, about 8% of the human genome is made up of various poorly understood HERVs. How they are transmitted — whether they are somehow infectious or are transmitted only through genetic inheritance — is unknown. HERVs are believed to have originally entered the DNA of microbes and have spread to the human genome, potentially through evolutionary rather than infectious routes, he said.

MS-associated retroviral element (MSRV), a member of the HERV-W family, is normally latent in the genome of susceptible individuals. But it plays a fundamental role in MS disease development when activated by co-factors.

GeNeuro has data from an epidemiology study of blood samples from 85 MS patients showing that 72% expressed high levels of the MSRV/HERV-W envelope protein (ENV) antigen, while ENV was not detected in any of 26 normal volunteers.

"ENV is conserved among all known HERV-W retroviruses and thus has very few mutations and large conserved domains — particularly those involved in receptor binding domains," Perron said, potentially making it a good therapeutic target.

Studies by other groups have correlated HERV viral load with MS progression. For example, the amount of ENV found in patients who died from MS is several logs higher than that in controls, according to a January study in the *Journal of General Virology*, Perron said.

Another paper published in December 2006 in *Multiple Sclerosis* showed that increasing ENV concentrations correlate with increasing numbers of relapses and disease severity. GeNeuro (Geneva, Switzerland) also is aware of unpublished data from another group of academic researchers, which show that geographic prevalence of HERV-W correlates with geographic prevalence of MS. The data are expected to be published this year.

Beyond this evidence of correlation, Perron believes ENV is responsible for the inappropriate immune response that attacks myelin and causes neurodegenerative MS flares. ENV has a "superantigenic effect on the human immune system," he said, leading to CNS inflammation.

GeNeuro has used HERV-W to induce an MS-like condition in mice. Traditionally, mouse models of MS are created using the immunotoxin Mycobacterium tuberculosis, which causes autoimmunity that results in T lymphocytes entering the CNS and attacking myelin. "We can reproduce this same autoimmunity by replacing the Mycobacterium tuberculosis with HERV-W," Perron said.

When these mice were treated with a MAb against ENV, MS-like symptoms were prevented from appearing, Perron said.

The company has not yet tried treating mice that have developed MS-like symptoms. But GeNeuro's anti-ENV antibody would most likely be used to treat MS attacks rather than prevent them, Perron said, because that is when the retrovirus is replicating and high levels of ENV are present.

"But that does not preclude us from pursuing prevention strategies later," he added.

Mopping up ENV would remove the source of inflammation, hopefully preventing damage and inducing remission. Other strategies such as prophylactic use of antibodies or anti-ENV vaccines also could be possible down the line, Perron said.

An anti-ENV antibody is slated to enter Phase I testing in 2009, and GeNeuro is working with BIM on a diagnostic that will help select patients for its trials and be used for monitoring efficacy. "We think the presence of ENV could be more predictive than MRI" as an indicator of MS inflammation and progression, Perron said.

GeNeuro is filing patents for other undisclosed neurodegenerative disorders that may be caused by HERVs, according to Jesus Martin-Garcia, a GeNeuro board member and partner at Eclosion.

In most cases, GeNeuro hopes to take its products through to the end of Phase IIa proof of principle prior to partnering.

GeNeuro S.A.

Geneva, Switzerland

Technology: Antibodies against human endogenous retrovirus (HERV) antigens

Disease focus: Multiple sclerosis and other neurodegenerative or neuropsychiatric disorders

Clinical status: Preclinical

Founded: 2006 by Herve Perron, Eclosion S.A. and bioMérieux S.A.

University collaborators: University of Navarra, University of Wuerzburg, Centre Hospitalier Universitaire Timone, University of Sassari, Don Carlo Gnocchi Foundation, Group Hospitialier Mondor, Hopitaux Universitaires de Geneve, Centre de Transfusion Sanguine, INSERM, la Faculte de Medecine RTH Laennec

Corporate partners: bioMérieux S.A.

Number of employees: 4

Funds raised: CHF2 million ($1.6 million)

Investors: Eclosion S.A.

CEO: NA

Patents: 18 issued patent families covering the sequences of HERVs, their biological functions, their pathological activities and ways to block them