Archemix scientists have now developed RiboReporters able to detect very low concentrations of proteins, suitable for "protein PCR," says Epstein.

However, Archemix's future revenue may come from aptamer-based therapeutics. Short strands of nucleotides may seem unlikely drug candidates, but proof of principle has already been gathered by Eyetech Pharmaceuticals (New York). Eyetech in-licensed the aptamer EYE100, targeted against the extracellular protein vascular endothelial growth factor (VEGF), from NeXstar (subsequently acquired by Gilead), and has the product in phase 2/3 trials for the treatment of age-related macular degeneration.

Archemix has great hopes for other therapeutic aptamers, which, according to Epstein, are superior in several ways to monoclonal antibodies. Aptamers have low molecular weights and are therefore easier and cheaper to manufacture than larger biologicals. Moreover, once an aptamer has been selected *in vitro*, it requires little chemical manipulation to make it suitable for use as a drug *in vivo*. Archemix, it seems, is well positioned to offer monoclonal antibody developers some serious competition. *LF*

BioVex

Heavy-weight viruses for clearing cancers

Viruses have long been used in medicine: inactivated viruses are used prophylactically to boost immunity against infectious diseases. More recently, they have been investigated as living vectors for eradicating cancers (oncolytic viruses) and chronic infections, such as hepatitis and human immunodeficiency virus. To date, however, such therapeutic viral vaccines have not been easy to apply—the viruses often do not readily infect cells for therapeutic effects.

Gareth Beynon, chief executive officer of BioVex, claims that his company has a viable solution in the form of the virus that causes common cold sores—herpes simplex virus (HSV) type 1. "HSV is a large and complex virus and not many people were working on it," says Beynon. However, David Latchman and postdoctoral scientist Robert Coffin, while working at University College London, investigated the *modus operandi* of the virus and how it might be harnessed for medicine—and it is this intellectual property that now underpins BioVex.

Latchman and Coffin's appreciation of how HSV infects and commandeers host cells for its own devices allowed them to construct two platform vaccine technologies. In their OncoVEX system, HSV has been engineered so that it replicates in rogue cancer cells only. OncoVEX is injected directly into solid tumors, where it infects cancer cells, replicates in number, and bursts open the rogue cells—the basis of oncolytic viral vaccines. However, even though OncoVEX infects cancer cells better than do many other oncolytic vaccines, says Beynon, alone, it will not clear the cancer completely. So the researchers added genes encoding human immune-stimulating agents, beginning with GM-CSF. When injected into melanomas in mice, OncoVEX$^{GM\text{-}CSF}$ not only eliminated those tumors, but also shrank non-injected tumors on the other side of the body. Moreover, the vaccine appeared to re-educate the immune system to look out for future tumor growth. In theory, OncoVEX$^{GM\text{-}CSF}$ may not only help shrink cancers but also reduce the risk of metastasis, which leads to a poor prognosis for cancer patients.

HSV is a particularly valuable vector for the creation of vaccines because it can infect dendritic cells—the cells of the immune system that are key to detecting foreign proteins (antigens) and raising an appropriate immune response. However, wild-type HSV can "switch off" dendritic cells after infection, suppressing the host's ability to raise an immune reaction against the virus. In BioVex's second platform—ImmunoVEX—HSV's ability to inactivate dendritic cells has been eliminated, and the resulting virus can effectively re-educate the body's immune system to recognize foreign antigens. ImmunoVEX will be used as immunotherapy for metastatic cancers and chronic infectious diseases. Beynon says that this will have to be done *ex vivo*: patients will donate a blood sample, and their dendritic cells will be extracted, infected with ImmunoVEX carrying a few select tumor antigens, and re-introduced into the patients' bodies. In theory, the treatment should "re-sensitize" the body against cancer and chronic infections, which have become invisible to the host's immune system. Several other companies follow a similar approach, but use the entire cell extracts from tumors as the cancer vaccine (the patient-specific "autologous approach"). BioVex focuses on four or five crucial antigens—in its first product, a set implicated in most malignant skin cancers—providing a "generic," and possibly more cost-effective, therapeutic strategy.

BioVex founders Robert Coffin (left) and David Latchman.

BioVex has sufficient funds to take its first vaccine, OncoVex$^{GM\text{-}CSF}$, into phase 1/2 trials for the treatment of malignant melanoma and breast, colon, and head and neck cancers later in the year. On the back of the phase 1 results, BioVex intends to raise additional funding to launch phase 2 trials of OncoVex$^{GM\text{-}CSF}$. Next year, the company plans to begin its first clinical trial with ImmunoVEX for the treatment of malignant melanoma. BioVex also intends to generate revenues from collaborations with pharmaceutical companies, such as Aventis (Strasbourg, France) and AstraZeneca (London), which are currently testing the company's vector platforms. *LF*

Founded: February 1999
Founders: David Latchman and Robert Coffin
CEO: Gareth Beynon
Employees: 35
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Location: Abingdon, United Kingdom
http://www.biovex.com