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BIOWORLD® TODAY

FRIDAY
JANUARY 29, 2010

THE DAILY BIOTECHNOLOGY NEWSPAPER

VOLUME 21, NO. 19
SPECIAL REPRINT

More Oxygen, Please: NormOxys Targeting Disease Via Hypoxia

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It's long been known that oxygen deficiency leads to many diseases, so it makes sense that increasing the release of oxygen would lead to effective treatment.

"But to find a molecule that can actually do it has not been easy," said Martin Tolar, president and CEO of NormOxys Inc., a company founded in 2004 by scientists Claude Nicolau and Nobel laureate Jean-Marie Lehn.

Nicolau, who worked on the idea for about two decades, was inspired by the ability of migratory birds to fly so high and far.

Through his research, he discovered an allosteric modulator of hemoglobin, essentially "an endogenous protein change," which allowed for greater release of oxygen, Tolar told *BioWorld Today*.

Red blood cells, which transport oxygen, only release 25 percent of the oxygen they have bound – plenty for healthy tissues but insufficient for diseased conditions.

The problem with existing oxygen treatments such as hyperbaric chambers is that the increased oxygen output can spread to unwanted areas of the body, so what Nicolau and Lehn wanted to do was find a small-molecule approach that could specifically target allosteric sites on hemoglobin.

They ended up creating oxyrens, or oxygen-release enhancers, which are designed to actively transport into red blood cells and bind to those allosteric sites, thereby allowing twice as much oxygen to be released.

And results so far have been "dramatic," Tolar said, albeit only in animal models to date.

NormOxys recently filed an investigational new drug application for its first oxyren, OXY111A, and "we'll begin the first study in a month or so in healthy volunteers."

The company intends to pursue cardiovascular disease and cancer as its first indications.

In the cardiovascular space, the objective is pretty straightforward – congestive heart failure, for instance, results in the heart muscle being unable to pump enough blood for normal oxygenation, so the oxyren would aim at getting that oxygen delivery back to normal levels.

In cancer, the goal is to boost oxygen levels to actually fight the disease.

"Solid tumors are dependent on hypoxia, so stimulating that oxygen release" through various pathways, such as the hypoxia-inducible factor, vascular endothelial growth factor or apoptotic pathways, would "allow the body to clear out cancer in a natural way," Tolar said.

Perhaps the most exciting discovery, he added, is that the cancer cleared in animal models has not recurred. "If we can translate a fraction of that effect in humans, then we'll have something that can provide substantial benefit."

And oxyrens can be used in combination with chemotherapy.

"Once we normalize the hypoxia, which normalizes the vasculature, we can use much lower doses of chemotherapy," Tolar said.

Other applications for oxyrens include anemia, where they could prove just as efficacious, yet safer than erythropoiesis-stimulating agents, and in age-related macular degeneration.

For now, though, NormOxys, having only recently emerged from stealth mode, is concentrating its efforts in the cardiovascular and cancer spaces.

Over the next year, Tolar said the firm hopes to establish proof of concept.

After that, "we'll be starting business development activities," though he added that NormOxys' platform already has caught some interest from big pharma.

Since inception, the company has pulled in about $15 million from Index Ventures and has been able to keep its burn rate low by operating its research in incubator space in Strasbourg, France.

It has about a dozen employees, "though we work with 20 to 30 people through universities," Tolar said.

NormOxys recently established corporate headquarters in Wellesley, Mass. ■