Andes Biotechnologies
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Silencing noncoding RNA to universally treat cancer

By targeting noncoding mitochondrial RNA with antisense oligonucleotide drugs, Andes Biotechnologies is developing potential cancer therapies capable of inducing inhibition of cell proliferation and apoptosis.

According to the World Health Organization, an average of 14 million new cases of cancer are diagnosed each year[1], which collectively cause 8.2 million deaths per annum. This makes the market for new cancer therapies one of the largest in the pharmaceutical industry. Last year, $100 billion dollars were spent on cancer drugs in the United States[2], and the global market for an effective cancer drug is estimated to reach $150 billion by 2018[3]. The race is on not only to access the market but also to discover safe and effective therapeutics that extend the lives of people with cancer worldwide.

Despite being the focus of the international research community for decades, cancer continues to be the leading cause of death worldwide. Major components of the problem are the heterogeneity within tumor tissue and the complexity of the multiple biological pathways that are affected at different stages of disease diagnosis and treatment, which present major challenges to overcome. Progress in cancer treatment has been slow, despite the recently approved breakthrough therapeutics. Most of these new, targeted drugs offer marginal extension of life, and a few are curative, but none of them shows universally good efficacy against multiple cancer indications.

Targeting noncoding RNA: a promising approach to treat cancer

Andes Biotechnologies was founded in 2008 in Chile to research and develop innovative and effective treatments for cancer. The company has discovered two novel families of long noncoding RNAs: sense (S-RNA) and antisense noncoding (AS-RNA). Both are present in all human cells, are synthesized in the mitochondria and migrate to the nucleus. The proprietary technology developed by Andes Biotechnologies is based on oligonucleotide drugs that target the novel long noncoding regulatory RNA that is present in a variety of cancer indications (**Fig. 1**). Andes's antisense drugs induce the inhibition of cell proliferation and cell death by apoptosis by reducing the levels of AS-RNA in multiple primary tumor cells and cancer cell lines. Importantly, the same treatment has no effect on normal proliferating human cells. RNA silencing represents a promising approach to the selective inactivation of disease-relevant genes with a new class of therapeutic products that could potentially revolutionize cancer treatment.

Preclinical studies have treated mouse xenograft models—including induced human prostate, bladder, breast and melanoma tumors—with Andes's antisense oligonucleotide drugs. This research

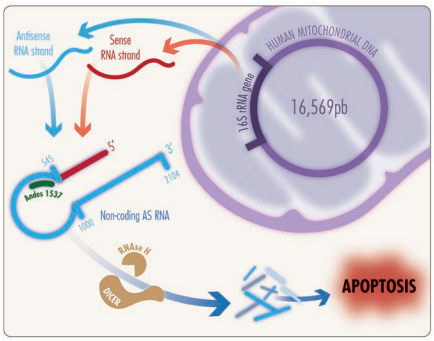

Figure 1: Diagram depicting the synthesis of the noncoding AS-RNA from the two strands of the 16S ribosomal RNA gene, the binding site of the Andes-1537 drug and the destruction of the RNA by the combined action of RNAse H and Dicer resulting in tumor cell death by apoptosis.

demonstrated a remarkable decrease in the rate of tumor growth compared to nontreated control mice. Preclinical data have also shown low or very low toxicity, and there is good evidence that several administration routes are possible for the antisense oligonucleotide drugs. Furthermore, these therapeutics help to eliminate relapse and metastasis in mice after the surgical removal of solid tumors, which results in long-term survival, whereas nontreated control animals are seen to relapse and develop metastasis within 10–12 days after surgery.

> **"Andes is reinstating the role of long noncoding RNAs in cancer biology**
>
> Cristián Hernández-Cuevas, Andes Biotechnologies

Andes Biotechnologies has an active investigational new drug (IND) application for phase 1 studies of its leading drug, Andes 1537. The aim of this first-in-human, open-label, dose-escalation and expansion, two-part study (NCT02508441) is to determine the safety and tolerability of its leading compound for injection into people with advanced unresectable solid tumors that are refractory to standard therapy or for which no standard therapy is available[4]. These studies are being carried out at the Cancer Center of the Mount Zion Hospital at the University of California, San Francisco, under the direction of Pamela Munster, professor of medicine and director of the early phase clinical program.

Partnership opportunities with Andes Biotechnologies

Andes Biotechnologies currently has a pipeline of 17 drug candidates that require further development, as well as an extensive portfolio of four patent families with more than 40 issued patents in several European countries, the United States, Japan, Mexico, Brazil and Chile. Many other patent applications are under prosecution in the same countries. The company is leveraging the value of its technology with a capable management team that has substantial experience in biotech product development, outstanding expertise in the mitochondrial and noncoding RNA field and a robust network of key national and international collaborations in the cancer research community. The company is using its preclinical efficacy and safety results and its strong intellectual-property portfolio—covering methods and pharmaceutical compositions—to seek partnerships or strategic alliances with biopharmaceutical companies for the codevelopment, launch and marketing of products for several potential cancer indications. Some indications may be treated as separate assets with the potential for additional partnerships or alliances. A trade sale is also a possibility. The company is funded through a combination of series A, series B and non-dilutive research grants.

1. http://www.who.int/mediacentre/factsheets/fs297/en/
2. http://www.nbcnews.com/business/economy/cancer-drug-spending-tops-100-billion-10-year-n353911
3. http://www.forbes.com/sites/matthewherper/2015/05/05/cancer-drug-sales-approach-100-billion-and-could-increase-50-by-2018/#49af8dfd70f4
4. Andes Biotechnologies. Phase 1 safety and tolerability study of Andes-1537 for injection in patients with advanced unresectable solid tumors. *ClinicalTrials.gov* https://clinicaltrials.gov/ct2/show/NCT02508441 (2015).

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