

Novel Oligonucleotides for Treatment of Human Cancer

Technology Summary

Human endogenous retroviruses (HERVs) are remnants of retroviruses that invaded and integrated into the human genome 6-15 million years ago. An important class of HERV retroviruses is ERV-9, which accounts for ~5% of the total human genome. The human genome contains approximately 50 copies of ERV-9 along with 3000-4000 copies of solitary elements of ERV-9 regulatory regions, called long terminal repeats (LTRs). The solitary LTRs contain promoter and enhancer elements that drive expression of genes located proximally to the LTR. Insertion of an ERV-9 LTR proximal to an oncogene could initiate carcinogenesis.

FDA researchers developed antisense and sense oligonucleotides (oligos) that target the RNAs of ERV-9 LTR as a treatment for various cancers, including human breast, liver, prostate, and myeloid cancers and fibrosarcomas. The inventors have shown the ERV-9 LTR sense and antisense oligos can inhibit cancer cell proliferation *in vitro* more efficiently than the antisense oligos of Bcl-2 (G3139) and telomerase (GRN163), both currently in cancer clinical trials. The oligos have minimal effects on the proliferation of primary normal human cells *in vitro*. The oligos also have potential as new therapeutic agents to suppress tumor cell growth, either when used alone or in combination with other antisense oligos or chemotherapeutic agents such as VePesid.

Potential Commercial Applications

- Therapeutic oligos may treat cancers including, breast, liver, myeloid and prostate cancers and fibrosarcomas.
- Oligos can be used alone or as adjuvant therapy with chemotherapeutic agents.
- ERV-9 LTR related cancers can be diagnosed by comparative analysis of the levels of ERV-9 LTR RNAs in tumors versus those of healthy tissues.

Competitive Advantages

- Greater inhibition of cell proliferation by oligos of the invention compared to the Bcl-2, telomerase and MDM2-specific antisense oligos which are currently in development as cancer therapies.
- The therapeutic effect of the oligos is specific for cancer cells as the oligos do not significantly alter proliferation of normal human cells.

Inventors: Lai Xu, Amy Rosenberg, Abdel Elkahoun, Fabio Candotti

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Product Area: Therapeutics, adjuvant therapy, cancer treatment, fibrosarcoma

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Licensing Contact:

Ken Millburne, J.D.
FDA Technology Transfer Program
Email: FDAINVENTIONLICENSING@FDA.HHS.GOV
Phone: 301-346-3964