

Versadel™ Oligonucleotide Technology for Bone Regulation

New advances in the understanding of the biology of bone growth have allowed the development of genetic therapies for encouraging bone growth where desired or inhibiting bone growth where undesired. Ablitech, Inc. has developed a new gene delivery technology called Versadel™ and currently has \$8M in grants planned to evaluate its use for the prevention of heterotopic ossification (bone growth in soft tissues) with the Department of Defense. Similar Versadel™ therapies could be adapted to other bone regulation strategies.

Background

Ablitech, Inc. develops radical methods for healing the human body by combining cutting edge knowledge in polymer science, molecular biology, and medicinal chemistry.

In June 2009, Ablitech filed for patent protection on:

- Method for protecting oligonucleotides for systemic delivery
- Successful delivery of protected oligonucleotides into cells
- Functionality of these oligonucleotides in the target cells

Highlights

Differentiated from current therapeutic delivery technologies:

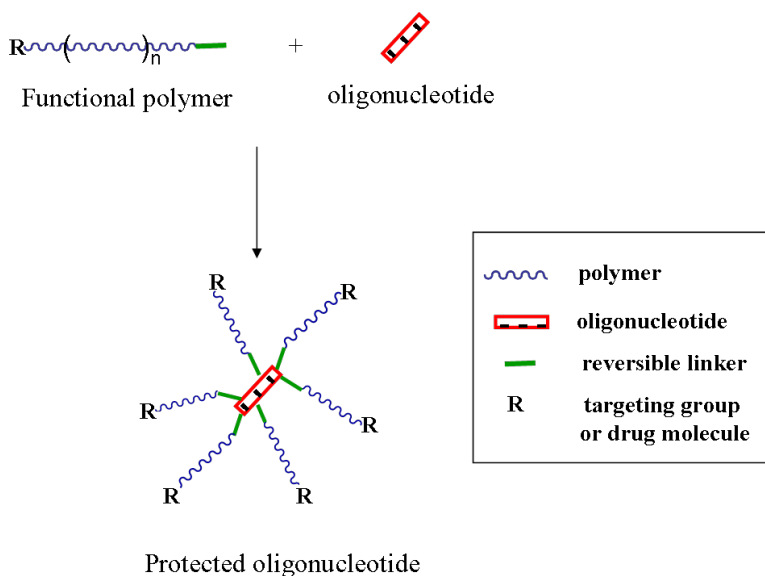
- NOT encapsulation technology - means no leakage
- Minimum 48 hours of protection in serum and other enzymes
- Non-toxic delivery system
- Clean process which fully restores active oligonucleotides in the cell
- Delivery designed to protect outside the cell and NOT reduce efficacy in the cell

Transaction

Ablitech has successfully completed initial laboratory trials using Versadel to treat cancer under a Phase I SBIR and is seeking partners to pursue animal testing. We are currently looking for partners for development of Versadel™ antisense oligonucleotides for bone regeneration.

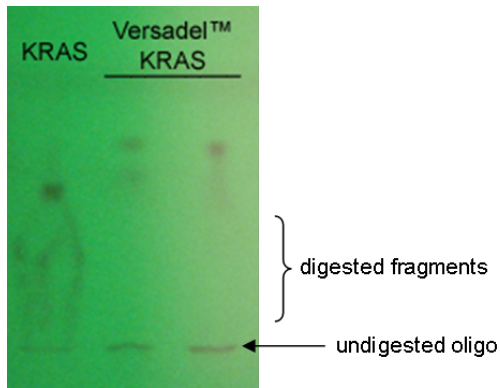
How It Works

A thin shell of protection is created by linking a hydrophilic polymer, such as polyethyleneoxide, to the oligonucleotide using very selective chemistry which reverses once inside the cell.



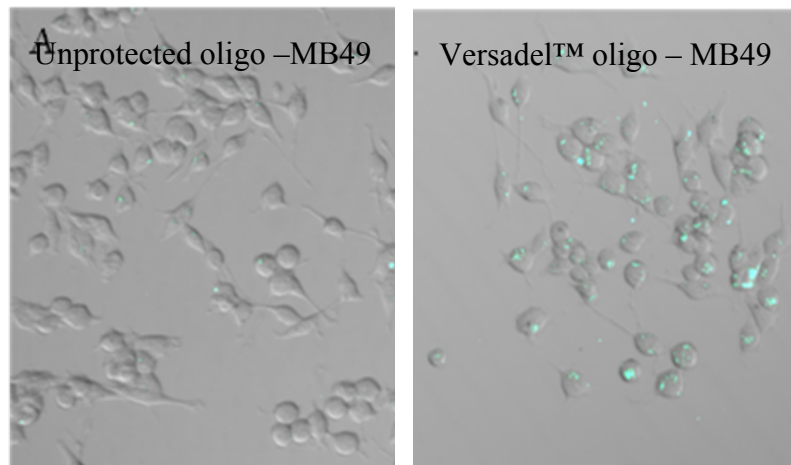
Data on Delivery to Cancer Cells

Several enzyme and serum solutions have been used to study the stability of Versadel™ oligonucleotides. As shown below, Versadel™ Kras (antisense oligonucleotide) was fully stable (undigested) at **48h in DNase I solution (30 units)**.

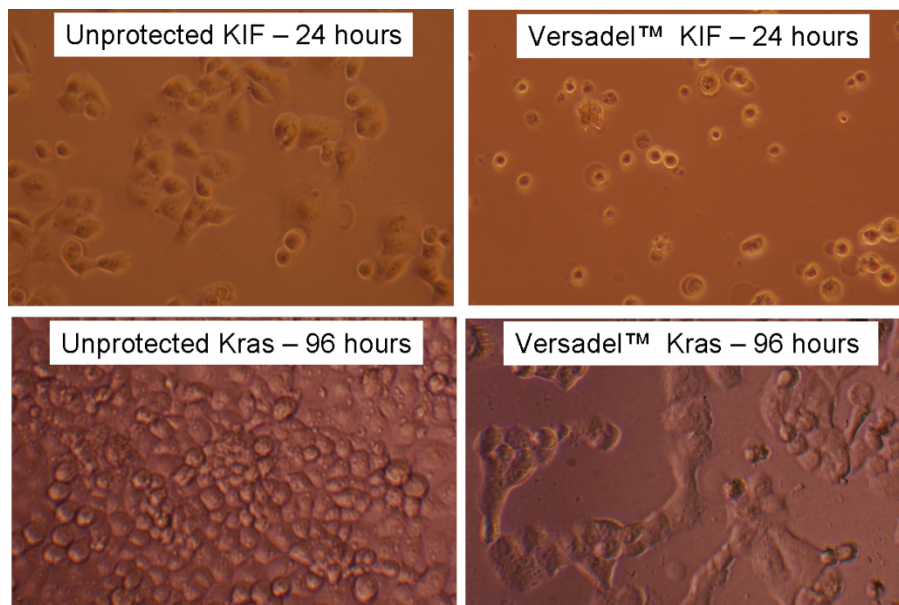


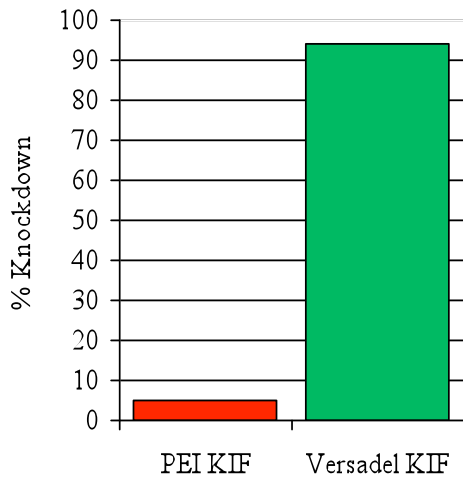
TLC under UV showing DNase I digestion studies after 48 hours. Samples shown are the unmodified Kras and two modified Versadel™ Kras oligos.

Uptake into mouse bladder cancer cells (MB49) has been demonstrated. MB49 cells (right) were exposed for 20h to a fluorescent-labeled unprotected oligonucleotide and a fluorescent-labeled Versadel™ oligonucleotide. This shows that the Versadel™ oligonucleotide was successfully transported into the cells.



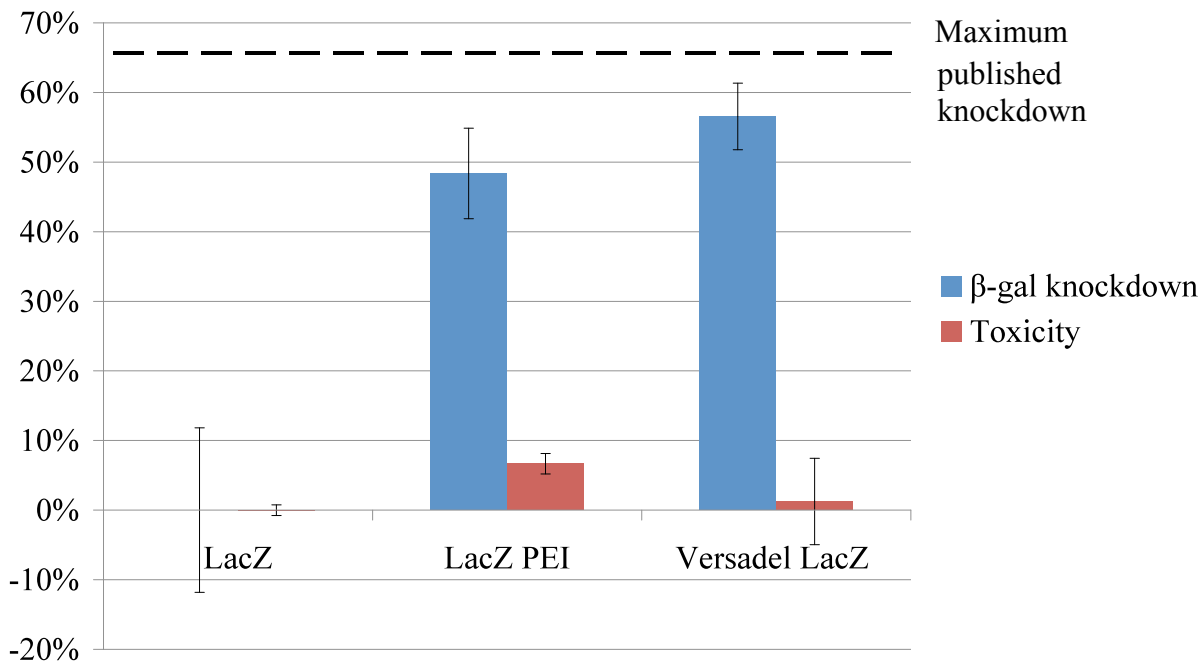
Versadel™ oligonucleotides showed **functional response in pancreatic cancer cells** (below). KIF blocks cell division and causes a “rounded-up” appearance, and Kras stops the cells from growing. This shows that the Versadel™ oligonucleotides were taken into the pancreatic cancer cells and were released once inside the cells in a fully functional form – proving our system is reversible.





Knock-down efficiency for Versadel™ KIF oligonucleotide at 10 μM exposed to MB49 cells over 24 hours. Ablitech, Inc.'s Versadel™ system showed nearly 95% knockdown versus the traditional PEI delivery system.

Functionality was also demonstrated using an oligonucleotide designed to knock-down a specific enzyme stably expressed inside the cell (the oligo was not intended to harm the cell or inhibit its growth). Versadel™ LacZ AS oligo showed 57% knock-down (this is substantial considering that the highest literature reported knockdown for this antisense sequence is 67%) in only 96 hours of exposure with 99% cell viability; this demonstrates our system is **functional without toxicity**.



Knock-down efficiency and cell viability data for Versadel™ LacZ AS oligonucleotide at 10 μM exposed to 9L/LacZ cells (rat brain tumor) for 96 hours.

For further information and to discuss potential partnerships, please contact:

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