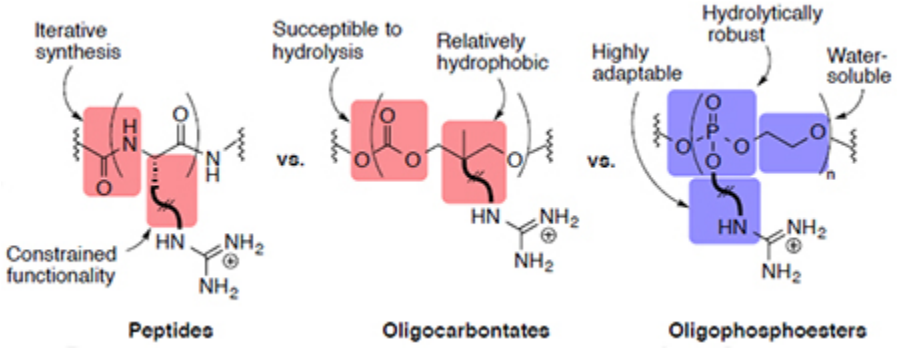
Docket #: S15-370

Cell-Penetrating, Guanidinium-Rich Oligomers for Drug and Probe Delivery

Stanford researchers have synthesized a highly effective molecule to transport drug conjugates across cell membranes. The molecular transporter can deliver either imaging probes or drugs as active conjugates or release the active agents upon uptake into targeted cells and tissues (e.g. cancer cells, stem cells, tumors, or infections). Delivery is effective in human cells and tissues, as well as other organisms including bacteria, algae, and plant cells. This molecular transporter is an oligomer with a phosphotriester backbone and functionalized side chains. The molecule can be tuned for a variety of therapeutic delivery and imaging applications.



Comparison of select oligomeric scaffolds for drug delivery. The highly effective Oligophosphoesters are shown in purple.

Applications

- **Molecular transporters** for end user applications in:
  - **Drug Delivery** – delivering bioactive therapeutic agents, nanoparticles, or biodegradable time-release materials
  - **Diagnostic Imaging** – delivering an imaging probe (fluorescent, magnetic, PET agent) as the cargo molecule.

Advantages

- **Increased Efficacy** of Transport Molecules
  - Penetrate new barriers including the blood brain barrier, algal cell wall, bacterial cell membrane and/or cell wall, skin, etc.
  - Demonstrate 2-3-fold higher uptake than guanidinium-rich oligocarbonates and 7-fold higher cellular uptake of cargo than oligoarginines.
  - Increase treatment efficacy when used as visualization of surgical procedures.
  - Localize in the mitochondria, increasing efficacy of mitochondria targeted drugs.
- **Biodegradable, Non-toxic Components** - Very well tolerated compound with tunable biodegradability for variable release of transporter-cargo conjugates.
- **Stable**
  - Stable in neutral buffer of > 25 days compared to half-life 8 hours for other oligomeric drug delivery.
  - Improved hydrolytic stability could enable commercial handling, storage, and transport in aqueous solution.
- **Tunable Water Solubility and Hydrophobicity** - Optimal hydrophilic/hydrophobic balance that allows for free solubility in aqueous media, and maintains hydrophobic character to allow membrane association and cellular uptake. The solubility and hydrophobicity of the cargo can be tuned to the desired properties.
- **Easy synthesis** -Oligomers can be synthesized in a single, metal-free oligomerization step.

Publications

- McKinlay CJ, Waymouth RM, Wender PA."Cell-Penetrating, Guanidinium-Rich Oligophosphoesters: Effective and Versatile Molecular Transporters for Drug and Probe Delivery." *JACS* 2016 Feb 22;10.1021/jacs.5b13452

Patents

- Published Application: WO2017083637

- Published Application: 20180319825
- Published Application: 20200308200
- Issued: 10,654,875 (USA)
- Issued: 10,961,263 (USA)

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