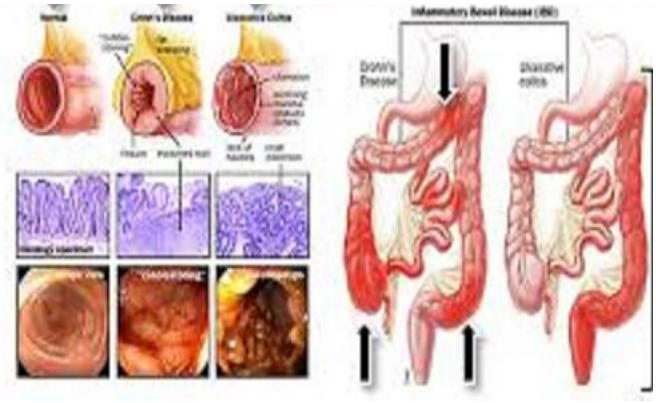
Phospholipid-Based Prodrug for the Treatment of IBD

The global inflammatory bowel diseases (IBD) drug market is estimated at $9.5bn in 2020 with novel therapies expected to be the main drivers of growth. Current IBD therapies target a particular segment in the gastrointestinal tract (GIT), generally the colon, regardless of where the inflammation is actually localized, thereby having a less optimal activity with high none specific effect.

The Technology

We propose a novel targeted therapy that delivers the anti-inflammatory drug specifically to the inflamed area. This is achieved by using a prodrug that contains an anti-inflammatory drug such as diclofenac linked by a carbonic linker to a phospholipid at the specific *sn*-2 position. Once the prodrug reaches the inflamed site it is cleaved at the *sn*-2 position by phospholipase A2 (PLA2), an enzyme that hydrolyses the *sn*-2 position of phospholipids (PL) and is overexpressed in the inflamed tissues of IBD patients. We have shown that activation of the prodrug and the release of the free drug from the complex depends on the design and length of the linker. Thus we demonstrated that, orally delivered PL-based prodrugs which release the free drug specifically at the diseased site(s) are an effective treatment of intestinal inflammation. For selecting the best and most effective prodrug we have developed a state of the art computational approach that simulates the PLA_2-mediated activation of different prodrugs. Based on the computational simulation, we have successfully synthesized a variety of PL-drug conjugates which upon in-vitro testing showed an excellent correlation to the computational simulations. Furthermore, using the selected prodrug, we were able to demonstrate high in-vivo local activation of the PL-Drug conjugate in a rat IBD model as compared to a minimal activation and drug release in healthy control animals.



Advantages

- ✓ The technology is based on approved drugs with validated activity.
- ✓ The technology enables higher efficacy and lower toxicity providing overall better patient care and therapy.
- ✓ The same rationale can be applied to other drugs for IBD.

Patent Status

Patent pending

Research Team

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