THE HARTWELL FOUNDATION

2015 Individual Biomedical Research Award

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Anti-inflammatory Nanomolecules for the Treatment of Crohn's Disease

Crohn's Disease is an inflammatory bowel disease associated with chronic swelling and irritation of the intestines. It is currently recognized as one of the challenging chronic diseases that affect children and adolescents. Symptoms include diarrhea, rectal bleeding, and abdominal pain, growth failure, malnutrition, pubertal delay, and bone demineralization. In the U.S. approximately 80,000 children are affected by this disease, and numbers are increasing yearly. The cause of Crohn's Disease is unknown. Treatments range from oral medications to injectable drugs that circulate widely throughout the body and inhibit inflammation. More than two-thirds of those with Crohn's Disease will require surgery during their lifetime, often drastically affecting quality of life. Pervasive challenges include depression, negative body image, social stigma, and a negative impact on family lifestyle. Unfortunately, front-line therapies are toxic to normal cells and as a consequence have multiple side effects, including an increased risk of cancer. Moreover, treatments for children with Crohn's Disease are based poorly on the safety and effectiveness of drugs in adult population. The important unmet need is for safe and effective treatments that specifically meet the needs of pediatric patients. Arun recently developed anti-inflammatory molecules that improve wound healing and seeks to adapt these to develop effective new treatments for children with Crohn's Disease. His proposed innovation is to engineer self-assembling peptides (short chains of amino acid molecules) that have both hydrophilic (water-loving, polar) and lipophilic (fat-loving) properties in a process where the individual components coalesce to form larger, highly ordered structures resembling high surface-to-volume nanofibers. Potent anti-inflammatory bioactive peptide recognition sites on the nanofiber surface can be designed to interact with tissue cell surface receptors or for binding to other biomolecules in order to achieve biological function, in vivo. He expects that the nanofibers will specifically target inflamed areas in the intestine so that a high proportion of the treatment will directly treat the affected area, minimizing systemic exposure of the drug and avoiding any undesirable side effects. He will evaluate the effectiveness of his approach in a pre-clinical mouse model of Crohn's Disease. If successful, Arun will have created a highly translatable treatment option for pediatric Crohn's Disease with a vast improvement over currently available oral medications. This will manifest itself in the form of either direct application of the molecules to the point of tissue injury, or through targeted systemic delivery.