CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
R1212

Project Title:
Recruitment of First-Time, Tenure-Track Faculty Members

Award Mechanism:
Recruitment of First-Time, Tenure-Track Faculty Members

Principal Investigator:
Siegwart, Daniel

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Dr. Daniel J. Siegwart received his Ph.D. in Chemistry from Carnegie Mellon University (CMU) in 2008 under the guidance of Professor Krzysztof Matyjaszewski. He then joined the lab of Professor Robert Langer at the Massachusetts Institute of Technology (MIT) as a National Institutes of Health sponsored postdoctoral fellow. Dr. Siegwart's research focuses on advanced polymeric systems with precise control over macromolecular architecture, order, and responsiveness for applications in drug delivery, bioengineering, and cancer.

At CMU, Dr. Siegwart studied Atom Transfer Radical Polymerization (ATRP) and utilized this technique to carefully construct functional biomedical architectures. Polymers are all around us, but it has traditionally been difficult to control how atoms add together into a chain to form a polymer because the process happens so quickly. Radicals are generated, and monomers (polymer building blocks) add every millisecond, forming long chains. ATRP is a special method that is able to extend the lifetime of the growing chain from one second to minutes, or hours, or even days. Now, because there is more time to do chemistry, new things suddenly become possible. one can control how the polymer forms, making new architectures and introducing new functionality that has led to totally new (bio)materials and applications.

During his graduate studies, Dr. Siegwart combined ATRP with radical ring-opening polymerization to produce temperature-sensitive "smart" polymers and hydrogels for bone fracture repair that were both injectable and degradable. He developed a synthetic route towards tri-block copolymers that could self-assemble into micelles for hydrophobic anti-cancer drug delivery. Dr. Siegwart also developed ATRP in inverse miniemulsion to form nanogels capable of delivering a variety of encapsulates. One particularly interesting result was that precise tuning of nanogel structure could enable encapsulation and controlled release of gold nanoparticles, doxorubicin, or proteins from within the gel network. Carefully immobilizing nanogels inside of a hydrogel system allowed for dual release of drugs at different times. These projects, among others, illustrated the power of advanced polymerization techniques to control architecture, functionality, and responsiveness in biomedical applications.

In the middle of graduate school training, Dr. Siegwart was awarded a fellowship from the National Science Foundation that allowed him to study at the University of Tokyo with Professor Kazunori Kataoka. In Tokyo, he worked on new methods to synthesize block

copolymer micelles that can localize to tumors inside of mice and deliver anti-cancer drugs. This fellowship further strengthened his desire to use his knowledge of polymer chemistry to work on projects that would improve health. At CMU, Dr. Siegwart was awarded the Joseph A. Solomon Memorial Fellowship in Chemistry and graduated with a Ph.D. in 2008.

In order to apply his background in polymer chemistry to translational medical applications, Dr. Siegwart conducted his postdoctoral research with Professor Robert Langer at MIT and focused on combinatorial, high- throughput methods in material discovery. He directed a project reporting the first large library of 1,536 structurally defined core-shell nanoparticles that established the key chemical guidelines for designing polymers for siRNA delivery. This enabled elucidation of complexation, internalization, and delivery trends that could only be learned through evaluation of a large library. Using structure-function analysis, cross-linkers optimally possessed tertiary dimethylamine or piperazine groups and buffering capacity. Covalent cholesterol attachment allowed for transfection in vivo to liver hepatocytes and blood monocyte/macrophages in mice. While at MIT, Dr. Siegwart also worked on the automated synthesis of non-fouling zwitterionic materials for cell encapsulation to treat diabetes, injectable materials to treat spinal cord injuries, and catalyst development for the automated synthesis of thiol-functionalized polymers for siRNA conjugation. His research on RNAi delivery has established key guidelines for designing materials for polymer-based siRNA delivery, and positions him to lead a laboratory focused on developing next-generation cancer therapies.

At the University of Texas Southwestern Medical Center in Dallas, Dr. Siegwart's long-term goals are to develop new materials for miRNA and siRNA delivery, develop new polymers to deliver chemotherapeutic drugs to hypovascular tumors, and to globally understand how the physical and chemical properties of materials affect interactions with biological systems in vitro and in vivo in the context of improving cancer therapies. He aspires to build upon all of his experiences to make a beneficial impact on human health through improved cancer therapies.