Published in final edited form as:

Clin Immunol. 2015 September ; 160(1): 1–2. doi:10.1016/j.clim.2015.07.006.

Nanotherapeutics for autoimmunity becomes mainstream

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Ten years ago, the concept of nanotherapeutics for autoimmunity would have faced significant challenges for even pre-clinical consideration from a broad array of entities; from federal and private funding bodies, to large size, internationally-operating pharmaceutical companies. Five years ago, this thinking changed and today, nanotherapeutics for autoimmunity is receiving increased consideration and support as the technology matures, becomes amenable to target product profile-based quality-by-design, and most importantly, demonstration of pre-clinical efficacy. On the one hand, the technology and the polymer biochemistry behind it has evolved and has spawned some quite clever and very imaginative approaches to formulate a diverse array of therapeutics, from small drugs, to biologics, to nucleic acids and intact genomes [1, 2]. An increasing interest in targeting particular cell populations promises to bridge the gap between systemic untargeted delivery and site-specific, cell-specific drug release [1, 2]. As the polymer biochemistry matures, so have the fields of fundamental biology.

Tremendous advances have been made in understanding immune regulations in the past decades. In cancer immunotherapy, the capacities to amplify immune responses generated from intrinsic or extrinsic means have yielded game-changing novel therapeutics for malignancies [3]. At the same time, new tools for downregulating immune responses have emerged rapidly in pre-clinical settings and many are being tested in humans. The advent of cellular and molecular tools aimed for suppressing immune responses have shifted the paradigm from global immunosuppression to antigen-specific tolerance induction as the end-point. Significant obstacles, however, remained in translating emerging molecular technologies to clinical modalities. Bystander effects and complex redundancies of immune mechanisms impose degrees of precision that are not possible with conventional formulations. To target relevant pathways driving disease pathogenesis without sensitizing bystanders, therapeutic entities must be delivered with spatiotemporal precisions. Nanomedicine may provide an answer in meeting the threshold [4].

We responded to the challenge to assist in the publication of a first-in-kind special issue devoted to nanotherapeutics in autoimmunity with the foreknowledge that this would be a pioneering work in the sense that it would open the door to many questions, while leaving even more unanswered. Yet, this is a challenge we eagerly accepted, as science and knowledge moves forward, and solutions to medical problems are solved only when more questions are asked and previously-unaddressed areas of investigation are brought to light.

In this theme issue, we selected a series of papers in which translational gaps may be met by materials science and bioengineering approaches. The foci of the current collection exemplify the notion that dampening immune-mediated tissue damage can be achieved by exploiting physical features of nanoscaled materials platforms (Hlavaty et al., this issue). These include polymeric particles (Engman et al., Fisher et al., Lewis et al., and Serra and Santamaria, this issue), exosomes (Thanh-Huyen et al., this issue), nanoemulsions (Patel et al., this issue), polymeric prodrug (Ren et al., this issue) and engineered cellular scaffolds (Tajima et al., this issue). The advantages lie in the ability of such entities to avoid rapid renal elimination, penetrate through interstitial space, and enter through plasma membrane efficiently. For type I diabetes (Engman et al., Figueroa et al., Lewis et al., this issue), inflammatory gut diseases (Ren et al., Thanh-Huyen et al., this issue), and allograft rejection (Fisher et al., Hlavaty et al., this issue), antigen-presenting cells (APCs) occupy a centerpiece of the complex immune cascades. Represented chiefly by macrophages and dendritic cells, APCs are targeted because their primary roles in inflammation and steering effector responses (Hlavaty et al., this issue). Polymeric nanoparticles are preferentially taken up by APCs, thereby concentrating the effects of the drug in these cells. Such formulations have particular utilities for biological agents; DNA (plasmid or anti-sense oligonucleotides) and siRNA can be protected from degradation, thereby extending exposure and increasing probability of contact. Enhanced bioavailability of T cell inhibitors, for example rapamycin and tacrolimus, results from micro- and nanoparticle formulations. Proven anti-inflammatory drugs, such as dexamethasone and celecoxib, can be reengineered to enhance target tissues accumulation, and as theranostics (Patel et al., this issue). Cellular therapies may render complex immunological signals that one or a few agents cannot provide (Tajima et al., this issue).

Nanomedicine is on the verge of becoming a common reality in the clinic. Merging multifunctional delivery platforms with targeted immune regulators may render pharmacodynamic and pharmacokinetic synergisms beyond what have been conceived thus far. This theme issue thus highlights opportunities for rational convergence of biological and physiochemical approaches in precise tuning of immune dysfunctions. We thank the reader for the time they may allot to the papers in this issue, as we seek their understanding that the many questions the research compels require further work to incisively address.

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