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EDITORIAL

CTI special feature on inflammatory diseases: a translational perspective

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Immune homeostasis relies on fine-tuned responses aimed at defending the host, protecting it from infection and promoting repair from injury. However, this process can go amiss, resulting in the development of inflammatory diseases. Despite very different aetiologies and clinical presentations, recent research findings in the physiopathology and treatment of inflammatory diseases prompt us to consider them as a whole. These are chronic, often incapacitating and painful illnesses that may have initiated in an acute localised manner, but progressed into systemic manifestations and destroy organs. In many cases, our understanding of inflammatory disease biology is limited, and available therapies vary greatly in their efficacy and safety. In this Special Feature of *Clinical and Translation Immunology*, leading exponents of inflammatory disease discuss the development of anti-inflammatory treatments in their respective fields and describe the efforts into translating results from promising preclinical animal studies to novel therapeutic strategies for humans.

Oon *et al.*[1] begin the issue by examining current and emerging therapeutics in systemic lupus erythematosus (SLE), namely those that target type I interferons or related signaling pathways. Monoclonal antibodies targeting IFNα have completed phase II clinical trials and an antibody against the type I interferon receptor is entering a phase III trial. Intriguingly, other interferons, such as IFNγ, and the more recently discovered type III interferons, are also emerging as targets in SLE. Blockade of upstream components of the interferon signaling pathway may also permit inhibition of more than one interferon subtype, and thus present as possible targeted therapy in this highly heterogeneous disease.

Our understanding of inflammation and inflammatory diseases has come a long way in the past decades, allowing for the development of effective anti-inflammatory therapies for diseases such as rheumatoid arthritis. However, it is becoming clear that a frequent side effect of anti-inflammatory therapies is perturbations in cholesterol homeostasis. Kraakamn *et al.*[2] present a new perspective on this topic and discuss the relationship between modulation of inflammation, hematopoietic subpopulation balance and metabolic risk factors for cardiovascular disease.

Immune cells are decorated with adrenoceptors to respond to signals mediated by the autonomic nervous system. In fact, the sympathetic nervous system (SNS) has been implicated in cancer progression and blockade of these adrenoceptors have been identified as a novel strategy to limit metastasis. Kim *et al.*[3] describe how neural signaling regulates metastasis and how SNS signaling regulates both biochemical and mechanical properties of tumour cells, tumour-associated immune cells and inflammation. Altered mechanotype is an emerging hallmark of cancer cells that is linked to invasive phenotype and treatment resistance. This article also discusses the potential for clinical translation of our knowledge of cancer mechanobiology to improve diagnosis and treatment.

Animal model is a powerful tool for fundamental research and discovery of new pathogenic factors and therapeutic targets. However, to successfully convert preclinical findings into meaningful outcomes in the clinics, novel pathways, mechanisms and treatments must be translated into human studies and applications. Kim *et al.*[4] use asthma as an example disease to discuss how murine models can be utilised in the discovery of novel mechanistic or functional targets for the development of therapeutic interventions for a difficult-to-treat form of asthma. These models recapitulate the hallmark features of the human disease and can be used to elucidate novel disease mechanisms and identify new therapeutic targets in severe asthma. Importantly, the authors propose similar approaches can be used in other diseases.

The discovery of invariant natural killer T (iNKT) cells and synthetic glycolipid analogues to modulate their activities has created a new research area aimed at the use of these cells for immunotherapy. Despite successes in mouse models, the translation of these results to non-human primates and humans has been challenging. Carreño *et al.*[5] provide a thorough discussion on the design of synthetic glycolipid activators for iNKT cells, their impact on adaptive immune responses and their use to modulate iNKT cell responses to improve immunity against infections and cancer. In addition, current challenges facing iNKT cell researchers in translating results from promising preclinical animal studies to humans will also be discussed.

The increasing incidences of inflammatory disease have had immunologists striving for an explanation. Proposals of how early childhood hygiene, widespread antibiotic use and the increase in processed food and lack of fibre consumption culminates in what was an under-appreciated part of us: our microbiota. The suggestion that shifts in the composition of host microbiota is a risk factor for inflammatory disease raises, an exciting opportunity whereby the microbiota may also present as a potential modifiable component or therapeutic target for inflammatory diseases. Shen *et al.*[6] provide insights into the interactions between the microbiota and the immune system, how these affect disease phenotypes, and explore current and emerging therapies that target the gut microbiota as potential treatment for inflammatory diseases.

Systemic infection and inflammation is commonly associated with platelet aggregation and adhesion within the microvasculature. In fact, disseminated intravascular coagulation is a frequent complication in sepsis that is associated with worsening of clinical outcomes and higher mortality in patients. However, patients who receive anticoagulants to treat the uncontrolled clotting often result with mixed outcomes. This is partly because therapeutic design of anticoagulants must be aware of the critical importance when 'uncoupling' platelet immunity from coagulation, whereby a complete inhibition of the platelet response cripples the host immune system. Davis *et al.*[7] describe the current array of anticoagulants and discuss the importance in recognising the intricate crossroads between inflammation and coagulation for future therapy development in infection-associated coagulopathy.

Translational research has become increasingly popular in recent years. Within the field of medical research, animal models are considered valuable research tools that provide insight into the complex world of human diseases, but they often lead us to ignore the possibility that these studies may only provide limited translational potential to humans. However, our understanding of inflammatory disease aetiology will be enhanced in the coming years through utilisation of emerging technologies and multiple omics platforms. By embracing big data and integrating host genetics with longitudinal proteomics, metabolomics, immune cell phenotyping, microbiome and clinical data, the extent to which host genetics and host-environment interactions modulate immune responses, disease susceptibility and response to therapy may become apparent. Therefore, future insights into inflammatory disease can be accelerated by unbiased approaches aimed at assessing the immune response, although, in parallel, investigating mechanistically how these factors modulate immune homeostasis in preclinical models.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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1 Oon S, Wilson NJ, Wicks I. Targeted therapeutics in SLE: emerging strategies to modulate the interferon pathway. *Clin Trans Immunol* 2016; **5**: e79.
2 Kraakman MJ, Dragoljevic D, Kammoun HL, Murphy AJ. Is the risk of cardiovascular disease altered with anti-inflammatory therapies? Insights from rheumatoid arthritis. *Clin Trans Immunol* 2016; **5**: e84.
3 Kim T-H, Rowat AC, Sloan EK. Neural regulation of cancer: from mechanobiology to inflammation. *Clin Trans Immunol* 2016; **5**: e78.
4 Kim RY, Rae B, Neal R, Donovan C, Pinkerton J, Balachandran L *et al*. Elucidating novel disease mechanisms in severe asthma. *Clin Trans Immunol* 2016; **5**: e91.
5 Carreño LJ, Saavedra-Ávila NA, Porcelli SA. Synthetic glycolipid activators of natural killer T cells as immunotherapeutic agents. *Clin Trans Immunol* 2016; **5**: e69.
6 Shen S, Wong CHY. Bugging Inflammation: role of the gut microbiota. *Clin Trans Immunol* 2016; **5**: e72.
7 Davis RP, Miller-Dorey S, Jenne CN. Platelets and coagulation in infection. *Clin Trans Immunol* 2016; **5**: e89.