understand temporal patterns among relevant autoantibodies and the IFN signature in relation to disease flares. Our data suggest a potential role for microbial triggers in driving the immune system activation that leads to disease flares and support activation of the type I IFN as highly associated with disease flare in many patients.

Learning Objectives
- Describe potential mechanisms of type I IFN induction in SL
- Describe individual temporal patterns in immune system activation based on longitudinal patient data
- Explain possible interpretations of longitudinal patient data with regard to triggers of lupus flare

REFERENCES

Type I interferon (IFN) is a potent substance. As such, the induction, transmission and resolution of the type I IFN-mediated immune response are tightly regulated. The type I interferonopathies represent discrete examples of a disturb-ance of the homeostatic control of this system due to Mendelian mutations, and their molecular definition has the potential to dissect fundamental aspects of IFN control in the human context. Of note, the recognition of type I inter-feronopathies is becoming of increasing clinical importance as treatment options are developed based on an understand-ing of disease pathology and innate immune signaling. Defini-tion of the type I interferonopathies to acquired autoimmune interferonopathies, of which SLE is the archetype. Evidence of activation of the IFN system through increased expression of sets of IFN-regulated genes, known as the IFN signature, was first detected in SLE over 20 years ago. Other evidence for the role of IFN in SLE includes exacerbation of animal models of lupus by IFN treatment and induction of lupus-like clinical phenotypes in humans treated with IFN for other diseases.

Early clinical trials of IFN-blocking therapies had limited success, associated with incomplete suppression of the expression of IFN signatures. More recently, a monoclonal antibody to IFNAR, anifrolumab, demonstrated efficacy in a Phase 3 trial, after prior success in Phase 2 and positive results against all but the primary endpoint in another Phase 3 study.1–3 Broadly, anifrolumab treatment resulted in reduced disease activity, improved skin, joint and flare outcomes, and increased rates of glucocorticoid tapering, with acceptable safety notwithstanding included increased rates of herpes zoster reactivation.4

The potential applications of IFN blocking treatments in the management of systemic lupus erythematosus (SLE) driven by this evidence base will be explored.

Learning Objectives
- Describe the phenotype breadth of the type I interferonopathies
- Describe the molecular basis of the type I interferonopathies
- Describe the status of interferon signalling in the type I interferonopathies
- Describe the clinical link between the type I interferonopathies and SLE
- Describe the link between the molecular pathology of the type I interferonopathies and SLE

REFERENCES