

Keynote Lecture

KE-1

THE STATS: A BRIEF REVIEW AND A BIT THAT'S NEW

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Our understanding of cell communication with the outside world until the mid-1980's was limited to the knowledge that MMTV responded transcriptionally to steroids and that second messengers – cyclic AMP, diacylglycerol and Ca⁺⁺ flux – somehow were connected to changed cellular behavior. Since that time the era of transcriptional control secondary to polypeptide occupancy of cognate cell surface receptors (the field which most attendees at this conference pursue) has blossomed. We will take a brief look at the breadth of the field and comment on its importance but question why it is indeed as limited as it is. In an attempt to keep up some standing as a practitioner of the art, discuss new results will be discussed from our now quite small laboratory on the activation-inactivation cycle of STAT1 and the possible utilization of STAT3 protein interactions in illuminating targets for cancer therapy.

KE-2

CYTOKINE CONTROL OF LYMPHOCYTE NUMBERS, ITS ROLE IN B CELL MALIGNANCIES AND INITIAL EXPLORATIONS OF THE ROLE OF RNA INTERFERENCE IN LYMPHOCYTE DIFFERENTIATION

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While the control of peripheral T cell numbers is still poorly understood, there is clear evidence that in the B cell compartment the survival of mature follicular and marginal zone B cells depends on, and is limited by, the interaction of a TNF family cytokine, BAFF, produced by non-B cells, with BAFF receptor (BAFF-R) on the B cell surface. BAFF-R signals through the NFB signaling pathway, and in vivo evidence demonstrates that all known functions of BAFF-BAFF-R interaction can be replaced by constitutive NFB activity. B cell lymphomas have to escape BAFF control by stromal cells, and appear to do so by at least two alternative mechanisms, namely cell-autonomous BAFF production or constitutive NFB activation, which in addition to overcoming BAFF dependency dramatically enhances the B cell response to mitogenic stimuli.

A second part of the talk will address initial insights into the role of RNA interference (RNAi) in lymphocyte development, using cell type specific ablation of components of the RNAi machinery or the ablation or over-expression of individual micro-RNAs. The emerging results indicate a crucial role of this new layer of control in key processes of T and B cell differentiation, including the differentiation of naïve T cells into Th1 and Th2 cells.