# Plenary Lectures

## Lectures

## PL.1

### Hematopoiesis and innate immunity: an inseparable couple for good and bad times, bound together by an hormetic relationship

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Hematopoiesis is regulated by several growth factors, cytokines, and chemokines, whose biological effects have been studied for many years. However, recently other mediators have been identified that affect the fate of hematopoietic stem/progenitor cells (HSPC) as well as non-hematopoietic cells residing in the bone marrow microenvironment. These novel mediators comprise members of the soluble arm of innate immunity, e.g., the complement cascade (ComC) cleavage fragments C3a and C5a and crucial members of purinergic signaling that are extracellular signaling nucleotides eATP and eAdo. Recent evidence accumulated that innate immunity in cooperation with purinergic signaling modulate several aspects of hematopoiesis and in response to low doses of potential stressors operating within the so called "hormetic zone" these interactions may benefit HSPCs. Moreover, for many years it was envisioned that components of innate immunity are exclusively synthesized in the liver. However, novel data from our laboratory indicates that they are also expressed by normal HSPCs and as a part of "complosome" regulate in an intracrine-dependent manner trafficking, proliferation and metabolism of HSPCs. Based on this a novel picture emerges how hematopoiesis is regulated both in steady state conditions as well as during stress - being regulated in coordinated manner by mediators of innate immunity and purinergic signaling.

## PL.2

### Regulatory RNAs encoded by bacteriophages

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Small regulatory RNAs (sRNAs) occurring in bacteria have a profound impact on various processes such as virulence, colonization ability, motility, and cell growth or death. When considering the significance of small regulatory RNA molecules encoded by bacteriophages phages, it becomes evident that they play a crucial role in the development of both the phage and its host. Regarding phage biology, they play vital roles during the early stages of infection, maintaining the state of lysogeny and suppressing the expression of late structural genes. The 24B_1 small non-coding RNA molecule has been identified in Escherichia coli after induction of Shiga toxin-converting bacteriophage Phi24B. We focused on its direct role during the phage and its bacterial host developments. We observed that in many aspects, this phage 24B_1 sRNA resembles herpesviral microRNAs. Similar to the herpesviral microRNAs, the mature 24B_1 is a short molecule, consisting of just 20 nucleotides. It is generated by cleaving the 80-nt long precursor transcript, and likely it undergoes a multistep maturation process in which the Hfq protein plays an important role, as confirmed by demonstration of its binding to the 24B_1 precursor, but not to the 24B_1 mature form. Moreover, similar to herpesviral microRNAs, the 24B_1 sRNA plays a significant role in maintaining the prophage state and reprogramming the host's energy metabolism. This study highlights importance of bactertiophage microRNA-size transcripts.

# PL.3

## Structural biology then and now – examples from the past half-century of progress

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Methods employed in the field of structural biology in general, and in investigation of protein structures in particular, have undergone tremendous changes in the last half-century. Introduction of synchrotrons as radiation sources for protein crystallography and the development of sophisticated computational approaches led to the ability to determine macromolecular structures in seconds rather than years, although by no means all structures can be solved that quickly. In the last ten years cryo-electron microscopy (cryo-EM) has been largely supplanting crystallography as a technique of choice for studies of protein structures, at least for larger proteins and their complexes. I will illustrate these changes by examples of work from my laboratory – studies of anticancer drug L-asparaginase that were initiated in mid-1970s and of Lon proteases that commenced 20 years ago. I will also mention the use of other techniques that helped in providing better understanding of the structure-function relationships for these important enzymes.