Cell and Microbiology

Alexander von GABAIN

o.Univ.Prof., Dr. (Heidelberg, Germany 1978)



Research

Our section is subdivided into three independent groups, concerned with the interface between microbes and mammalian defense cells: We study the growth, activation and differentiation of macrophages and the adjustment of bacteria to stress and environmental changes. All projects study systems where rapid changes in gene expression are instrumental. We also analyze bacteria- and virusmediated aberrations of the immune system.

A von Gabain

RNA decay in bacterial and mammalian cells

The stabilities of different mRNA species in a given cell span a wide range and RNA decay is an important element in the regulation of gene expression. Particularly micro-organisms modulate the level RNA turnover in response to different

environments which may be brought about by changes in growth conditions or invasion of eukaryotic tissues. Ribonuclease RNase E is one of the enzymes performing the rate-limiting steps of mRNA degradation in bacteria. We have now detected an endonucleolytic activity in human cells which processes E. coil RNAs with the same specificity as RNase E from E. coll.

Recently we have identified an RNA binding complex in E. colf that provides physical protection against RNA degradation by endoribonucleases. To our surprise this complex contains GroEL as an indispensable constituent. This protein, which has well known functions as a chaperonin in protein folding, appears to be the first 'RNA chapero.

T Decker

How macrophages develop into mature cells that function in the immune system

Macrophages perform a variety of functions in the regulation of an immune response. Moreover, they contribute to the body's natural immunity through their ability to phagocytose and destroy infectious micro-organisms. Macrophages develop from immature bone marrow cells through a complex series of precursor stages.

We are studying the molecular signals telling macrophages to develop into mature cells in response to hormone-like substances that bind to the cell surface. Our particular focus is on those signals that reprogram gene expression, so that the newly expressed genetic information enables a macrophage precursor cell to become a functionally mature and differentiated cell.

M Baccarini

Molecular mechanism underlying growth and differentiation in macrophages

Macrophages represent an excellent model system for studying cell growth and differentiation because of their ability to proliferate or differentiate in response to various stimuli. As in other experimental systems, cytosolic kinases of the MAP-Kinase type participate in these biological processes. The activation of these kinases in macrophages, however, depends on a pathway distinct from previously described ones.

We have identified new intermediates in this alternative pathway, and are in the process of clarifying its further steps. Our work underscores the diversity and combinatorial nature of signal transduction in mammalian cells, in which analogous signalling intermediates can be rearranged to form different pathways.

Teaching

Members of the section teach molecular microbiology, cell biology and immunology, from introductory to highly advanced courses. Laboratory courses deal with microbes and their enviroment, immune cell biology, and protein-nucleic acids interactions and protein modifications.

International Cooperations

Alexander von Gabain is adjunct professor of the Karolinska Institute in Stockholm. All three senior group leaders maintain active collaboration with groups in Europe and the USA.

Selected References

- Büscher D, Hipskind RA, Krautwald S, Reimann T, Baccarini M(1995) Ras-dependent and independent pathways target the MAP-Kinase network in macrophages. Mol Cell Biol 15: 000
- Eilers A, Baccarini M, Horn F, Hipskind RA, Schindler C, Decker T(1994) A factor induced by differentiating signals in cells of the macrophage lineage binds to the gamma interferon activation site. Mol Cell Biol 14: 1364-1373
- Eilers A, Decker T (1993) The response of the Gamma Interferon Activation Factor (GAF) is under developmental control in cells of the macrophage lineage. Mol Cell Biol 13: 3245-3254
- Georgellis D, Sohlberg B, Hart U, von Gabain A(1995) Identification of the chaperonine groEL as a constituent of an mRNA protection complex in *E. coli*. Molecular Microbiol 16: 1259-1268
- Wennborg A, Sohlberg B, Angerer D, Klein G, von Gabain A (1995) A human RNAse E-like activity which cleaves RNA sequences involved in mRNA stability control. Proc Nat Acad Sci USA 92: 7322-7326