8TH EUROPEAN
IMMUNOLOGY CONFERENCE

June 29-July 01, 2017 Madrid, Spain

Keynote Forum

Day 1

Euro Immunology 2017

Thomas Böldicke, J Clin Cell Immunol 2017, 8:3(Suppl)
DOI: 10.4172/2155-9899-C1-035

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Thomas Böldicke

Helmholtz Centre for Infection Research, Germany

Single domain antibodies for the knockdown of cytosolic and nuclear proteins

Single domain antibodies (sdAbs) from camels or sharks comprise only the variable heavy chain domain. Human single domain antibodies comprise the variable domain of the heavy chain or light chain. SdAbs are stable, non-aggregating molecules *in vitro* and *in vivo* compared to complete antibodies and scFv fragments. They are excellent novel inhibitors of cytosolic/nuclear proteins, because they are correctly folded inside the cytosol in contrast to scFv fragments. SdAbs are unique because of their excellent specificity and possibility to target posttranslational modifications such as phosphorylation sites, conformers or interaction regions of proteins that cannot be targeted with genetic knockout techniques and are impossible to knockdown with RNAi. The most frequently selected antigenic epitopes belong to viral and oncogenic proteins, followed by toxins, proteins of the nervous system as well as plant-and drosophila proteins. It is now possible to select functional sdAbs against virtually every cytosolic/nuclear protein and desired epitope using synthetic single pot single domain antibody libraries without the need of immunization. In summary, cytosolic/nuclear sdAbs of camelid, shark and human origin can be applied to clarify the function of uncharacterized proteins such as virus proteins and host cell factors, oncogenic proteins and cofactors, proteins of the nervous system, intracellular enzymes involved in signaling, transcription factors and proteins involved in differentiation and development.

Biography

Thomas Böldicke has obtained his PhD degree from Max Planck Institute of Molecular Genetics, Berlin. Since 1986, he has been working at Helmholtz Centre for Infection Research, as a Project Leader of Intracellular Antibodies.

thomas.boeldicke@helmholtz-hzi.de

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Liwei Lu, J Clin Cell Immunol 2017, 8:3(Suppl)
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Liwei Lu

University of Hong Kong, Hong Kong

Roles of regulatory B cells in autoimmunity

Extensive studies have demonstrated the prominent functions of B cells in antibody production and antigen presentation. However, certain B cell subsets have been recognized as immune regulators through cytokine production. Accumulating data indicate that IL-10-producing B cells possess a regulatory function in the development of autoimmune diseases, but microenvironmental factors and/or cytokines involved in inducing regulatory B cell differentiation remain to be identified. B cell-activating factor (BAFF), a member of TNF family cytokines, is a key regulator for B cell maturation and function. Our recent studies have identified a novel function of BAFF in the induction of IL-10-producing regulatory B cells. BAFF-induced IL-10-producing B cells showed a distinct $CD1d^{hi}CD5^{+}$ phenotype mainly derived from marginal-zone B cells, which possessed a potent function in inhibiting T cell activation and cytokine production. In mice with collagen-immunized arthritis and experimental Sjogren's syndrome, adoptive transfer of BAFF-induced IL-10-producing B cells markedly attenuated the disease severity and tissue damage of autoimmune diseases via suppression of Th17 cell response. Taken together, our findings have provided new insight in understanding the roles of BAFF and regulatory B cells in autoimmune pathogenesis, which may facilitate the development of therapeutic strategies for targeting autoimmune disorders.

Biography

Liwei Lu is an internationally recognized expert in the field of Autoimmunity. His research is focused on studying immune dysregulations in autoimmune diseases. During last ten years, his laboratory has been exploring novel strategies for the treatment of rheumatoid arthritis. His team was among the first to successfully treat autoimmune arthritis by targeting the cytokine B-cell activating factor in a preclinical study, which has significant therapeutic implications for the effective treatment of rheumatoid arthritis. He is the Councillor of Federation of Immunological Societies of Asia-Oceania and has served as the Chairman of Hong Kong Society for Immunology. He has published over 120 peer-reviewed papers in leading immunology and rheumatology journals.

liweilu@hku.hk

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Thomas Grundström

Umeå University, Sweden

Regulation of diversification and affinity maturation of antibodies

B-lymphocytes can modify their immunoglobulin (Ig) genes to generate antibodies with a new isotype and enhanced affinity. Activation-induced cytidine deaminase (AID) is the key mutagenic enzyme that initiates these processes. How somatic hypermutation (SH) and class switch recombination (CSR) are targeted and regulated is key to understanding how we achieve good antibodies. The *trans*-acting factors mediating specific targeting of AID and thereby SH and CSR have remained elusive. No direct coupling between a transcription factor and the specific targeting of AID has been demonstrated, and how AID is recruited is still a big mystery. We show that mutant E2A with defect inhibition by the Ca^{2+}-sensor protein calmodulin results in reduced B cell receptor- (BCR-), IL4- plus CD40 ligand-stimulated CSR to IgE. AID is shown to be together with the transcription factors E2A, PAX5 and IRF4 in a complex on key sequences of the *Igh* locus in activated mouse splenic B cells. Calmodulin shows proximity with them after BCR stimulation. Direct protein-protein interactions are shown to enable formation of the complex. BCR signaling reduces binding of the proteins to some of the target sites on the *Igh* locus, and calmodulin resistance of E2A blocks this reduction. Thus, E2A, AID, PAX5 and IRF4 are components of a CSR and SH complex that calmodulin binding redistributes on the *Igh* locus. We present also regulation of a "mutasome", the protein complex that enables repair at high error rate of the uracils made by AID on Ig genes but not on most other genes.

Biography

Thomas Grundström completed his doctorate at Umeå University in 1981 and his Medical degree in 1982. Dr. Grundström was post-doc 1982-1984 in the laboratory of prof. Pierre Chambon, Strasbourg, France, where he characterised the first discovered enhancer of transcription. He is professor at the department of Molecular Biology at Umeå University since 1994. Dr. Grundström discovered the first direct Ca2+/calmodulin inhibition of a transcription factor (Corneliusen et al., Nature, 1994) and has characterized the Ca2+ regulation of many regulatory proteins with a focus on the immune system. Dr. Grundström is presently studying regulation of production of high affinity antibodies.

Thomas.Grundstrom@umu.se

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Day 2

Roswitha Gropp, J Clin Cell Immunol 2017, 8:3(Suppl)
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Roswitha Gropp

Hospital of the LMU, Germany

The combination of disease modeling, immunological profiling and the NSG-UC animal model leads to a better understanding of the mechanism underlying inflammation in UC

One reason for the lack of individualized therapies in ulcerative colitis (UC) may be that the conventional approaches are not adequate to understand the complexity of chronic inflammatory diseases. They mostly rely on the identification of certain cell types and cytokines associated with the disease phenotype, followed by verification of their roles *in vitro* and *in vivo*. This approach does not take into consideration that the observed pathologies might be the result of different causes. In addition, inflammatory responses are highly dynamic processes that require the cross talk of the immune-, epithelial-, endothelial-, muscle cells, and fibrocytes. The conventional approach further disregards the high plasticity of T-cells and monocytes, which both have the capacity to adopt their phenotype depending on the inflammatory milieu. Therefore, we took a more comprehensive approach and developed FACS, ELISA and autoantibody panels to portray individual inflammatory profiles. In addition, we developed a disease map of UC by computational modeling. Finally, we developed an animal model which enables us to proof the hypothesis generated by modeling and profiling. So far, we tested infliximab, adulizumab, sirolimus, anti CD1a antibodies, anti CCR4 antibodies and the IL-4Rα /IL-13α1 inhibitor pitrakinra in our mouse model. Results suggest that the animal model is highly reflective of the human disease, that therapeutic responses can be predicted by the computational model and that novel therapeutics emerge from this approach.

Biography

Roswitha Gropp has over 25 years of experience in preclinical development and inflammatory diseases. She recently took on a different view considering the inflammatory process in UC as an uncontrolled wound healing process. This hypothesis assumes that epithelial damage induces the release of signals to evoke a Th2 characterized inflammatory response that ultimately results in repair of the colon. Using agent based modeling first disease maps were developed to describe the inflammatory milieu and the dynamics of the inflammatory response. This approach together with immunological profiling of patients allows for a better understanding of underlying mechanisms ultimately leading to individualized therapies.

Roswitha.Gropp@med.uni-muenchen.de

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