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Doctoral College
Metabolic & Cardiovascular Disease

Medical University of Graz
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DECODING LIGAND RECEPTOR INTERACTIONS

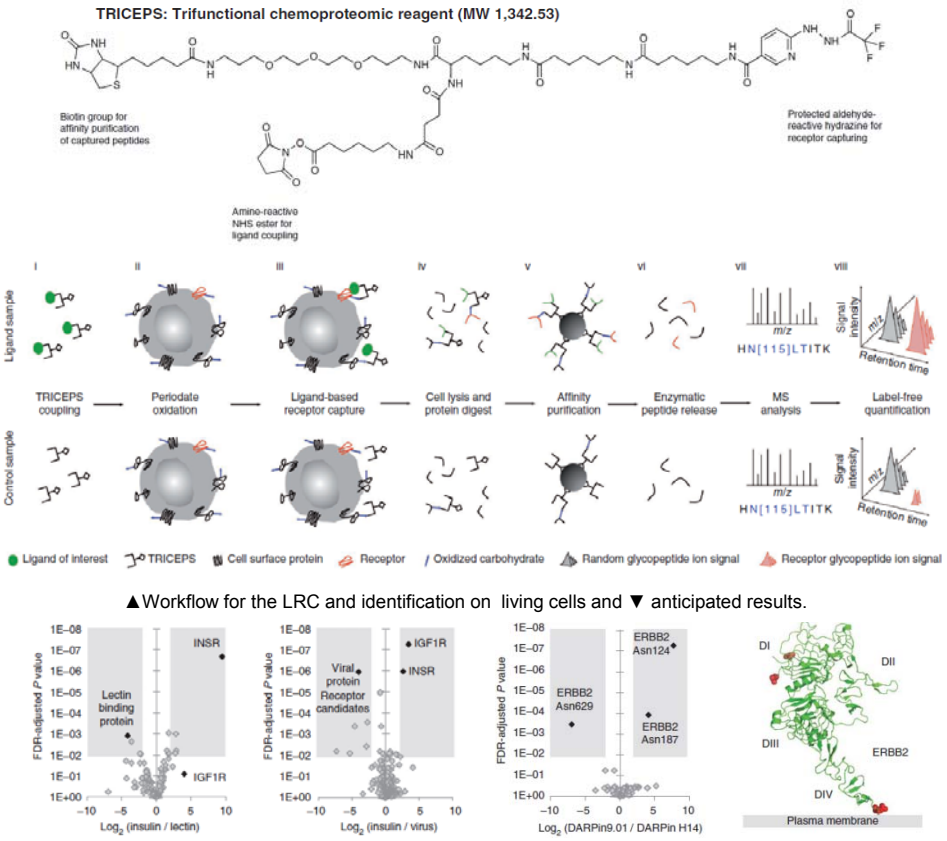
GUEST LECTURE by

Dr. Bernd Wollscheid

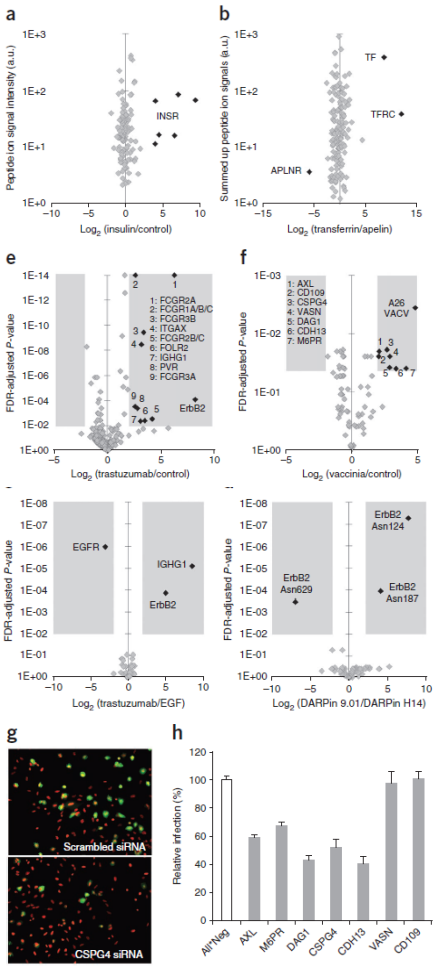
**Institute of Molecular Systems Biology,
ETH Zurich, Switzerland**

Thursday, 29.08.2013
17:00h

**Lecture Hall E1, Lecture Hall Centre
(Auenbruggerplatz 15), MUG**



▲Workflow for the LRC and identification on living cells and ▼ anticipated results.



LRC identifies receptors and receptor panels for ligands ranging from peptides to intact viruses on living cells and tissues.

Direct identification of ligand-receptor interactions on living cells and tissues.
Frei et al. (2013) Nat Biotechnol 30(10):997-1001

Ligand-based receptor identification on living cells and tissues using TRICEPS.
Frei et al. (2013) Nat Protocols 8(7):1321-1336

DECODING LIGAND RECEPTOR INTERACTIONS

Ligand-induced changes in cell surface receptors result in physiological responses, which constitute the biological activity of various ligands such as proteins, peptides, pharmaceutical drugs, toxins or whole pathogens. However, traditional approaches for the ligand-based identification of corresponding receptors are usually limited to non-transient, high affinity interactions and highly artificial experimental set-ups. Therefore, many signaling molecules remain orphan ligands without a known primary molecular target – invaluable information in understanding the respective mechanisms of signal transduction, drug action or disease.

Previously, we have developed the cell surface capturing (CSC) technology for the unbiased identification and quantification of cell surface N-glycoproteomes by mass spectrometry (MS), sets of SRM assays for selected N-glycopeptides of clinical interest and the Cell Surface Protein Atlas (CSPA). This demonstrated the powerful applicability of chemical reagents in the tagging of cell surface glycoproteins at carbohydrate groups and the subsequent purification of the corresponding peptides for MS analysis.

Based on these results we now synthesized trifunctional cross-linkers for the ligand-based tagging of glycoprotein receptors on living cells and the purification of receptor-derived peptides for MS analysis. Through quantitative comparison to a sample generated with an unspecific control probe, this ligand-based receptor capturing (LRC) approach allows for the highly specific and sensitive detection of ligand interactions with their corresponding receptors under near-physiological conditions. Experiments with ligands ranging from peptide hormones to clinical antibodies demonstrate the potential of this approach to specifically identify one or more target receptors for a given ligand with great statistical power. Advanced discovery-driven applications reveal potential receptors and receptor panels for ligands ranging from protein domains to intact viruses.

Together, I will present a short summary of our recent clinical research to understand the surfaceome as a cellular signaling gateway and a chemoproteomic technology for the unbiased detection of ligand-receptor interactions on living cells.

CURRICULUM VITAE

Dr. Bernd Wollscheid is a research group leader and head of the NCCR Neuro Center for Proteomics at the Swiss Federal Institute of Technology in Zurich, Switzerland. After studying chemistry in Freiburg and Boston he obtained his PhD in Molecular Immunology from the Max-Planck Institute for Immunobiology. His postdoctoral research took him to the Institute of Systems Biology in Seattle where he developed and applied chemoproteomic technologies to elucidate cell surface protein biology. Now at the Institute for Molecular Systems Biology at ETH Zurich he developed a research program focusing on a Systems Biology understanding of the cell surface as a cellular information gateway and on the identification of cell surface glycoproteins as diagnostic and therapeutic clinical targets.

2006 -	ETH Zurich, Institute of Molecular Systems Biology, Zurich, Switzerland
	Independent Research Group leader & Head of the NCCR Neuro Center for Proteomics
2005 – 2006	Institute for Systems Biology, Seattle, WA, USA
	Research Scientist
2002 – 2005	Institute for Systems Biology, Seattle, WA, USA
	Post-doctoral fellow, Laboratory Dr. Ruedi Aebersold
1997 – 2002	Max-Planck-Institut for Immunobiology, Freiburg, Germany
	Ph.D. Molecular Immunology, Laboratory Prof. Dr. M. Reth
1995 – 1997	Study of Chemistry; Albert Ludwigs University, Freiburg, Germany
	Major: Biochemistry; Thesis at the Max-Planck-Institute for Immunobiology/Freiburg; Prof. Dr. M. Reth
1993 – 1995	University of Massachusetts, Boston, MA, USA
	Scholarship from Baden-Württemberg/DAAD
1990 – 1993	Study of Chemistry; Albert Ludwigs University, Freiburg, Germany

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