

Protein Biophysics and Biochemistry group (Head: G. Fritz, [personal data sheet](#))

Our aim is to understand cellular processes at a detailed molecular level allowing targeted intervention and modulation of these processes. We study signaling proteins involved in neurodegenerative and tumorigenic disorders, with current focus on the the 3D structure determination of the cell surface receptor RAGE and its ligands from the S100 protein family. Moreover, we explore the challenging structures of respiratory complexes of pathogenic bacteria.

Personalia

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Research Topics

Structure of the receptor for advanced glycation endproducts (RAGE) and its ligands

RAGE is a member of the superfamily of immunoglobulin type cell surface receptors. In endothelial cells and immune cells RAGE activation is required for the perpetuation of the immune response, whereas in neuronal cells RAGE activation leads to neurite extension and stimulates neuronal survival. RAGE has the unusual property to bind a large range of different molecules such as advanced glycation end products (AGEs), β -sheet fibrils, and several S100 proteins. We investigate the unique structural properties of RAGE by X-ray crystallography and by NMR in collaboration with

[Prof. Walter Chazin](#)

. Our next goal is to resolve a RAGE-ligand complex at atomic resolution.

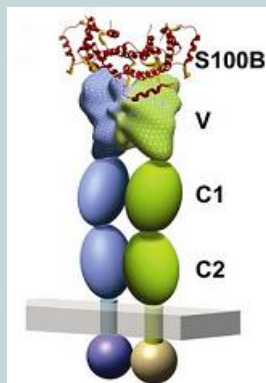


Figure: Modell of an active RAGE-ligand complex

References: Ostendorp T, Leclerc E, Galichet A, Koch M, Demling N, Weigle B, Heizmann CW, Kroneck PMH and Fritz G (2007) Structural and functional insights into RAGE activation by multimeric S100B. *The EMBO Journal* 26: 3868-3878

Leclerc E, Fritz G, Weibel M., Heizmann CW, and Galichet A (2007) S100B and S100A6 differentially modulate cell survival through their interaction with distinct RAGE (receptor for advanced glycation end products) immunoglobulin domains. *J. Biol. Chem.* 282, 31317-31.

S100 Proteins

The S100 protein family comprises 21 different members in human. Various diseases such as cardiomyopathies, neurodegenerative and inflammatory disorders, as well as cancer are associated with changes in expression patterns of the different S100 proteins. Several S100 proteins occur in the extracellular space where they act in a cytokine like manner through the receptor for advanced glycation end products (RAGE).

Intracellularly, S100 proteins function as Calcium (II) and Zinc (II) dependent regulators of cell division, cell growth, and motility. Some members of the S100 family bind also Copper (II) with high affinity.

We investigate the structural changes associated with metal ion binding and required for activation spectroscopic methods as well as by X-ray crystallography. Structures of S100 proteins in the inactive / active state and in complex with different signaling ions give insights into the molecular mechanisms of signal transduction.

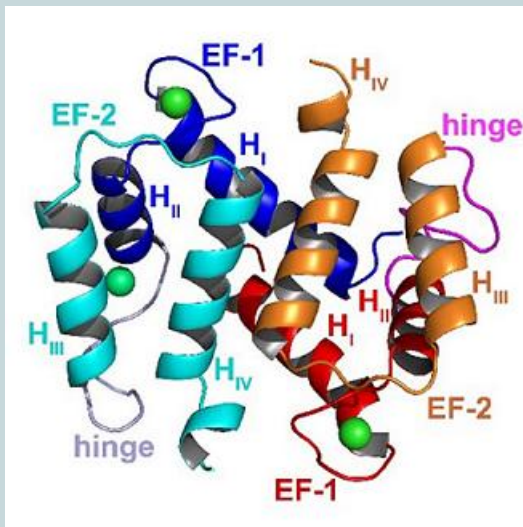


Figure: Structure of S100A2 apo

Koch M, Diez J, Fritz G (2008) The Crystal structure of human Ca²⁺-free S100A2 at 1.6 Å resolution. *J. Mol. Biol.* 378, 931-940

Leclerc E, Fritz G, Vetter S and Heizmann CW (2008) Binding of S100 proteins to RAGE: an update. *BBA Mol. Cell Res.* 1793:993-1007. (Review)

Marenholz I, Heizmann CW and Fritz G (2004) S100 proteins in mouse and man: from evolution to function and pathology. *Biophys. Biochem. Research. Commun.* 22:1111-1122. (Review)

Complex Redox Proteins

All organisms catalyze redox reactions and transform the liberated energy into chemical energy for growth, motility and reproduction. The proteins involved in energy transduction require specific co-factors like flavin or metal ions like iron organized in multiple core centers. The NQR protein complex of *Vibrio cholerae* is investigated in close collaboration with [Prof. Julia Steuber](#).

The properties of the redox co-factors are investigated by EPR spectroscopy and X-ray structure determination of soluble domains and of the entire complex are in progress.

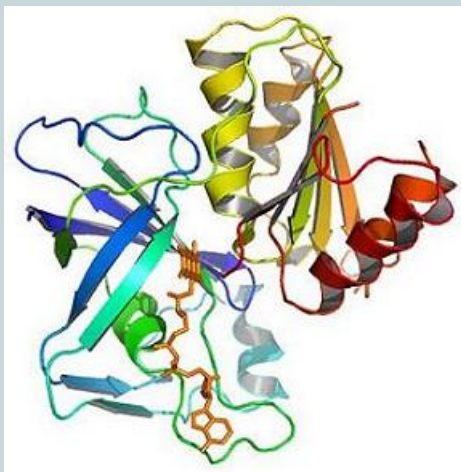


Figure: Structure of NQR subunit

Reference: Tao M, Fritz G, Steuber JM (2008) The Na⁺-translocating NADH:quinone oxidoreductase (Na⁺-NQR) from *Vibrio cholerae* enhances insertion of FeS in overproduced NqrF subunit. *J. Inorg. Biochem.* 102, 1366-72.

Fritz G, Einsle O, Rudolf M, Schiffer A, Kroneck PMH (2005) Key bacterial multi-centered metal enzymes involved in nitrate and sulfate respiration. *J. Mol. Microbiol. Biotechnol.* 10:223-33.(Review)