Structural basis of RAGE S100B interaction

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RAGE (Receptor for Advanced Glycation Endproducts) is a multi ligand receptor which binds proteins glycan-modified proteins, amyloid β and several S100 proteins, among them S100B. Our aim was to resolve the structural basis for the ability of RAGE to recognize structurally divergent molecules and in particular for its interaction with S100 proteins. We recently identified that S100B like S100A8/A9 [1] and S100A12 [2] forms non-covalent multimers, and characterized their binding properties and structural properties [3]. Several S100 proteins bind next to Ca(II) also Zn(II) with rather high affinity. We found that Zn(II) which occurs extracellularly in μ M concentrations modulates strongly S100-RAGE interactions, suggesting a further level of regulation. To characterize the counterpart of S100-RAGE interaction we determined the X-ray structure of RAGE ligand-binding domain at 1.85 Å resolution. The arrangement of the molecules in the crystal suggests a preassembly of the receptor during activation which is supported by our biochemical studies.





- [1] Korndörfer at al. (2007) J. Mol. Biol. 370: 887-898
- [2] Moroz OV et al. (2002) Acta Cryst. D58: 407-413
- [3] Ostendorp et al. (2007) Embo J. 26: 3868-3878