

Structural insights into iron(III) reduction by human STEAP4

Wout Oosterheert¹, Laura S. van Bezouwen^{1,2}, Remco N. P. Rodenburg¹, Joke Granneman¹, Friedrich Förster², Andrea Mattevi³ & Piet Gros¹

w.oosterheert@uu.nl

¹*Crystal and Structural Chemistry, Bijvoet Center for Biomolecular Research, Utrecht University*

²*Cryo-Electron Microscopy, Bijvoet Center for Biomolecular Research, Utrecht University*

³*Department of Biology and Biotechnology 'L. Spallanzani', University of Pavia, 27100, Pavia, Italy*

Enzymes of the six-transmembrane epithelial antigen of the prostate (STEAP) family reduce Fe(III) and Cu(II) ions to facilitate metal-ion uptake by mammalian cells. STEAPs are upregulated in several human cancers, making them potential therapeutic targets¹. However, the structural basis for STEAP-catalyzed electron transfer through an array of cofactors to metals at the membrane luminal side remains elusive. We present a single-particle cryo-EM study which provides structural insights into transmembrane electron transport and iron(III) reduction by human STEAP4 .

¹Hubert, R. S. et al. (1999), STEAP: a prostate-specific cell-surface antigen highly expressed in human prostate tumors. *Proc. Natl Acad. Sci. USA* 96, 14523–14528.