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Neutron Diffraction Structure of Fully Deuterated Aldose Reductase Shows a Proton Exchange Important for Catalysis. A. Podjarny¹, A. Mitschler¹, I. Hazemann¹, M. Blakeley², M.T. Dauvergne², F. Meilleur², M. Van Zandt³, S. Ginell⁴, A. Joachimiak⁴, D. Myles^{2#}, ¹IGBMC, Illkirch, France, ²EMBL, ILL, 38042 Grenoble, France, ³IDD, Branford, CT, USA, ⁴ Bioscience Div., SBC, ANL, Argonne, IL, USA, [#]Current address: CSMB, ORNL, USA.

Human Aldose Reductase (h-AR) is implicated in diabetic complications. Crystallisation trials, with fully deuterated enzyme (EMBL, Grenoble) complexed with NADP⁺ and the inhibitor IDD-594, succeeded. Neutron Laue diffraction measured on LADI (ILL, Grenoble) achieved a resolution of 2.2 Å at room temperature, even with a rather small crystal volume of only 0.15 mm³. The data collection statistics are good; e.g., the $\langle I/\sigma(I) \rangle$ value is 5.1, and the overall Rmerge is 22.8%. Growth of larger fully deuterated crystals is under way.

Neutron density maps showed clearly the deuterium atoms in the active site region. The protonation states, including that of the catalytic His 110, match those observed in the subatomic resolution X-Ray structure. There is additional information available from the neutron structure. For example, the polarization of Tyr48 by Lys77, important for the catalytic reaction, is confirmed by a proton (deuterium) channel between them.