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Structural and Biochemical Studies of the Tryptophan 2,3-Dioxygenase Reveal the Molecular Detail of Tryptophan Oxidation. Farhad Forouhar,¹ Ross Anderson,² Chris Mowat,² Sergey M. Vorobiev,¹ Mariam Abashidze,¹ Arif Hussain,¹ Seetharaman Jayaraman,¹ Chiara Bruckmann,² Sarah Thackray,² Todd Tucker,¹ Haleema Janjua,³ Rong Xiao,³ Thomas B. Acton,³, Gaetano T. Montelione,³ Steve Chapman,² Liang Tong^{1*}, ¹Dept. of Biological Sciences, Northeast Structural Genomics Consortium, Columbia Univ., New York, NY 10027, ²School of Chemistry, Univ. of Edinburgh, West Mains Rd Edinburgh EH9 3JJ. ³Center for Advanced Biotechnology and Medicine, Northeast Structural Genomics Consortium, Rutgers Univ., Piscataway, NJ 08854.

The essential but least abundant amino acid L-tryptophan is a precursor for serotonin, NAD/NADP, and polyADP-ribose. Tryptophan 2,3-dioxygenase (TDO) is a hemoprotein that catalyzes the first and rate-limiting reaction of tryptophan degradation via the kynurenine (KYN) pathway, by incorporating a dioxygen into the indole moiety of tryptophan. In mammals, more than 90% of the total tryptophan is degraded by TDO in the liver through the KYN pathway. The related enzyme, indoleamine dioxygenase, is a target for the treatment of cancer and autoimmune diseases. Here we present extensive structural and biochemical studies of the *Xanthomonas campestris* TDO and a related enzyme from *Shewanella oneidensis*. These studies provide molecular insight into the mechanism of tryptophan oxidation.