WWOX Oxidoreductase – Substrate and Enzymatic Characterization

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WWOX is a tumour suppressor gene that spans the common fragile site FRA16D. Analysis of the WWOX expression pattern in normal human tissues showed the highest expression in testis, prostate, and ovary. Its altered expression has been demonstrated in different tissues and tumour types. The WWOX gene encodes a 414-amino acids protein, which is the first discovered protein with a short-chain dehydrogenase/reductase (SDR) central domain and two WW domains at the NH₂ terminus. Due to its potential role in sex-steroid metabolism, using two bacterial expression systems, we have cloned WWOX fusion proteins showing oxidoreductase activity in a crude extract, defined a course of enzymatic reactions for selected steroid substrates, and determined related K_m values. Our results show that the SDR domain of the WWOX protein has dehydrogenase activity and is reactive both in the presence of NAD⁺ and NADP⁺ for all examined steroid substrates. On the other hand, with the same substrates and reduced cofactors (NADH and NADPH) reduction activity was not observed.

Key words: WWOX, Oxidoreductase, Steroid Metabolism