"Molecular and Clinical Aspects of Thyroid Hormone Transporters"

The action of thyroid hormone is largely determined by the intracellular T3 concentration, which is dependent on a) the serum level of T3 and its precursor T4, b) the local expression of deiodinases (D1-3) that catalyze the activation of T4 to T3 (D1,2) or the inactivation of both T4 and T3 (D3), and c) the activity of transporters which mediate the cellular uptake and/or efflux of T4 and T3.

Some tissues are supplied by circulating T3; in others T3 is locally produced from T4. This local T3 production may take place in the same cell where T3 acts (autocrine mechanism) or in adjacent cells (paracrine mechanism). The brain is an important example of the latter situation, where most T3 is produced from T4 by D2 expressed in astrocytes and supplied to adjacent neuronal targets. These neurons also express D3, which terminates T3 activity.

MCT8 is an important thyroid hormone transporter. Its gene is located on the X-chromosome. The pathophysiological importance of MCT8 has been demonstrated by the identification of different mutations in male patients affected by severe psychomotor retardation, also known as the Allan-Herndon-Dudley syndrome. These patients also have highly elevated T3, low T4, and slightly increased TSH levels. The neurological defect is explained by the lack of T3 transport into neuronal targets during brain development.

The highly homologous MCT10 protein also effectively transports iodothyronines in addition to aromatic amino acids but its physiological relevance remains to be established.