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pH Effect on Lead Transport into astrocytes by Divalent Metal Transporter 1(DMT1/Nramp2)

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Nramp2, also known as DMT1 and DCT1, is a 12-transmembrane domain protein responsible for dietary iron uptake as well as metal ions such as lead, manganese, zinc, copper, nickel, cadmium, and cobalt. High expression of DMT1 increase lead uptake, and DMT1-dependent lead transport was H -dependent and inhibited by iron ions. The molecular mechanism of lead transport in CNS is as yet unknown, although interactions between iron and lead at the level of absorption have been known for some time. The process of lead uptake into astrocytes was not known yet. Nramp2 may mediate transport of heavy metal into astrocytes.

We investigated whether Nramp2 mediate transport of lead into astrocytes. And we do whether Nramp2 was expressed highly by deprivation of iron in Astrocytes, and lead uptake into astrocytes was influenced by expression of Nramp2. Immortalized human fetal astrocyte(SV-FHA) cells were cultured in medium containing Dulbecco's modified Eagle's medium and treated with Deferoxamine. Northern blot analysis was done for determining mRNA level of DMT1 and lead uptake assay was done in incubation condition of pH 5.5 and 7.4.

Lead uptake into astrocytes increased time-, pH-, and concentartion-dependently, and was saturable. At pH 7.4 lead uptake was the highest level, but at pH 5.5 it represents properties of transport by Nramp2. Iron deprivation by the treatment of Deferoxamine increases mRNA level of Nramp2 in astrocytes. It was time- and concentration-dependent, and saturable. High expression of Nramp2 increase lead uptake into astrocytes in pH 5.5, but decrease in 7.4. Iron ions inhibit lead uptake in pH 5.5 but not in pH 7.4.

We may suggest that DMT1 in astrocytes functions also at a low pH, and is not major route of lead-transport.

Key word : DMT1(Nramp2), Lead transport, Deferoxamine, Astrocyte