[S4-1] [10/19/2001(Fri) 14:00-14:40 /Hall B]

## α-Tocopherol Transport Protein and Familial Isolated Vitamin E Deficiency

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α-tocopherol is absorbed from the diet into the intestine, then transported in the chylomicron lipoprotein fraction to the liver. It is then secreted by the liver into the circulation from where it is transported via the VLDL lipoprotein fraction to diverse peripheral tissues. In the liver, the cytosolic α-tocopherol transport protein (α-TTP) plays an important role in the intracellular transportation of α-tocopherol. α-TTP specifically binds α-tocopherol and is its main transporter between biological membranes.

We purified this protein 10 years ago, its molecular weight amounting to 31 kDa. α-TTP has a very high affinity to α-tocopgerol when compared to other tocopherol derivatives. This is especially interesting due to the fact that γ-tocopherol is the most abundant in the daily diet. When comparing the metabolism of α- and γ-tocopherol, it should be noted that α-TTP is necessary for the discrimination of α- and γ-tocopherol and transports preferentially α-tocopherol to peripheral tissues. The lack of α-TTP in the liver leads to a block in the transportation system of α-tocopherol and finally to a deficiency state in the peripheral tissues, although the intestinal absorption and transportation via the lipoprotein fraction are intact, α-TTP deficiency can be seen in humans as well as in mice. In humans, familial isolated vitamin E deficiency causes similar symptoms as in α-TTP knockout mice, which we have raised in our laboratory. After we primarily described a mutation in the human α-TTP gene in 1995, more than ten mutations causing isolated vitamin E deficiency have been found worldwide.

My talk will focus on isolated vitamin E deficiency caused by the lack of α-TTP.