Role of cholesterol in neurite outgrowth of cerebellar granule cells in vitro

Cholesterol is an important component of cell membranes. It regulates membrane fluidity, and forms lipid rafts together with glycosphingolipids. In the nervous system, besides its structural role in cell membranes and myelin, cholesterol is also involved in synaptogenesis and hedgehog signalling pathway. All cholesterol in the brain is made locally since plasma lipoproteins, the transporter of cholesterol in the blood circulation, are unable to cross the blood-brain barrier. In vivo observations have shown that the mice whose cholesterol synthesis in the cerebellar granule cells has been abolished do not have any phenotype. It could be because neurons are surrounded by enriched cell types, and their greatest demand for cholesterol synthesis is concentrated on certain development stage. I was interested on the role of cellular cholesterol synthesis in developing neurons under defined in vitro conditions. Squalene synthase (SQS) was the targeted enzyme we chose to block the cholesterol synthesis. It catalyzes the first committed step in sterol formation. In our study, we transfected Cre plasmids to delete the SQS gene in cultured cerebellar granule cells, which came from mice with LoxP sites flanked SQS gene. Therefore, the cholesterol formation in these cells was blocked. Cotransfected control plasmids successfully monitored cre-expression and showed the morphology of the transfected cells. We found that cholesterol-deficiency in cerebellar granule cells results in the inhibition of dendrite outgrowth and branching without significantly altering axonal elongation.