

NG2 is a transmembrane glycoprotein, which takes part in cellular processes such as adhesion, migration or invasivity, i.e., in processes important in tissue development but also in tumor and metastasis formation. Among other things, NG2 leads to an inhibition of neurite growth, and probably plays an important role in amoeboid type of cell invasion. These processes are in many respects similar. Both in inhibition of neurite growth and in mesenchymal-amoeboid transition occur morphological changes which lead to a loss of cell protrusions and a transition to a rounded shape. In both of these processes Rho/ROCK signaling also plays a crucial role. Connection between NG2 and the Rho/ROCK signaling pathway has been indicated in the process of inhibition of neurite growth. The mechanism of Rho/ROCK signaling regulation by NG2 glycoprotein is, however, still unknown. In this thesis is proposed a molecular mechanism of Rho/ROCK pathway activation by glycoprotein NG2 which relies on the NG2/MUPP1/Syx signaling complex where the scaffold protein MUPP1, bound to activated NG2, enables binding and activation of the Syx protein. Syx then as RhoGEF activates Rho/ROCK signaling, and the activated Rho/ROCK pathway leads to inhibition of neurite growth, increased cell contractility and traction forces. These processes are crucial for amoeboid type of cell invasion. It is also possible that NG2 functions as an integrin- substitute adhesion molecule. Glycoprotein NG2 might therefore be one of the crucial molecules which through activation of Rho/ROCK signaling and integrin-independent adhesion leads to amoeboid cell invasion.