Investigating Neurofibromin - Fbxo3 Interactions in Live Cells Using NanoBiT Technology

Won, Jinhee (School: Carmel High School)

Neurofibromatosis type 1 (NF1) is one of the most prevalent dominantly inherited diseases. It occurs in approximately 1 in 3000 people. NF1 encodes a tumor suppressor whose functional loss results in the development of neurofibromas, or benign tumors, that may progress to malignancy. NF1 is characterized by an haploinsufficiency of neurofibromin. However, little is known about the degradation pathways of neurofibromin. A previous experiment identified Fbxo3 as a possible candidate to mediate the ubiquitin-proteasome pathway (UPP) for neurofibromin. Fbxo3 is the recognizing subunit of the SCF-E3 complex. Thus, we investigate the interaction between Fbxo3 and neurofibromin. In neurofibromin, there are splicing isoforms with two suspected different binding sites of Fbxo3, Gap Related Domain 1 (GRD1) and Gap Related Domain 2 (GRD2). We demonstrate that Fbxo3 directly interacts with both gap domains of neurofibromin in live cells. This project implicates that Fbxo3 in SCF-type E3 ligase mediates the recognition of neurofibromin to cause polyubiquitination and degradation of neurofibromin.

Awards Won: