

## Purification, crystallization of proteins from an integrin-related signal transduction family

### Background

Kindlins constitute a family of evolutionarily conserved cytoplasmic components of cell–ECM adhesions that bind to  $\beta$ -integrin cytoplasmic tails directly and cooperate with talin in integrin activation. In addition, kindlins interact with many components of cell–ECM adhesions—such as migfilin and integrin-linked kinase—to promote cytoskeletal reorganization. Loss of kindlins causes severe defects in integrin signalling, cell–ECM adhesion and cytoskeletal organization, resulting in early embryonic lethality (kindlin-2), postnatal lethality (kindlin-3) and Kindler syndrome (kindlin-1). Kindlins are multi-domain proteins containing a FERM domain that targets to the cell membrane and a PH domain that binds to membrane phospho-lipids. Unlike other proteins containing these two domains, the FERM domain is interrupted by the PH domain suggesting that Kindlin-1 possesses a unique domain shuffling feature and may thus execute a specific biological function. For this, we are expecting the availability of the three-dimensional structure of this focal adhesion molecule and keen to see how this unique domain structure is spatially arranged.

### Project Description

In order for structural studies, one needs a good amount of purified protein for crystallization. To this end, we have made expression constructs for recombinant protein production in *E. coli*. This work is just at a preliminary state, but some positive results have been gained already, e.g. the expressed products are soluble. A master student, who is interested in working at our lab, will be recruited for this project. He/she will mostly work on purification optimization and/or subsequent crystallization trials, learn basic skills in molecular biology and structural biology, and may have an opportunity to go to ESRF, the largest synchrotron light source in Europe, in Grenoble, France for diffraction data collection.

### Contact person: Dr. WEI LIU

X-ray unit led by Prof. Rudolf Ladenstein  
Center of Structural Biochemistry  
Karolinska Institutet  
NOVUM 141 57 Huddinge

E.mail: [wei.liu@ki.se](mailto:wei.liu@ki.se)