# Functional and structural differences between Sorting Nexin 3 and Sorting Nexin 12

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M. Romano[I], **C. Lopez Robles**[II], M. Lucas[I], A. Rojas[I], A. Hierro[I]

[I]CIC Biogune, Bilbao, Spain, [II]CIC bioGUNE, Derio, Spain

Protein recycling is essential for cell homeostasis. Several systems have been developed to perform this process. Among them, Retromer, a heteropentameric protein, is involved in recycling of proteins (known as cargos) from late endosomes to Golgi apparatus or plasma membrane [1,2].

Retromer is composed of the Cargo Selection Complex (CSC), formed by Vps35, Vps26 and Vps29; and accessory proteins called Sorting Nexins (SNX). CSC was thought to be the unique responsible of cargo recognition, and mutations on its sequence causes severe diseases like Parkinson or Alzheimer [3]. Intense research has been done on Retromer and its interaction with cargos and SNX, and recent results prove the importance of both CSC and SNX for cargo recognition [1].

SNX are a family of proteins that contain a PX domain, able to recognize phosphoinsitides (PI), specially PI(3)P [4]. They are involved in protein-lipid interaction, specially in the endocytic network. A heterodimer of SNX1/2 and SNX5/6 was thought to be the putative partners of CSC, but recent results have demonstrated the interaction with others SNX, like SNX3, in cargo recognition and recycling [1].

SNX12 is a PX containing SNX highly similar to SNX3. Although it was thought to be expressed at low levels, recent results show high expression in mice brain [5]. Furthermore, based on the structure of SNX3 [1] and the not yet published SNX12 structure solved in our lab, we try to demonstrate differences in PIP recognition between SNX3 and SNX12, what would be a starting point to differentiate this two similar proteins, thought to be redundant in function until now. Furthermore, this result would open a new insight in SNX–CSC biology, implicating high relevance of SNX in cargo recognition and sorting.

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