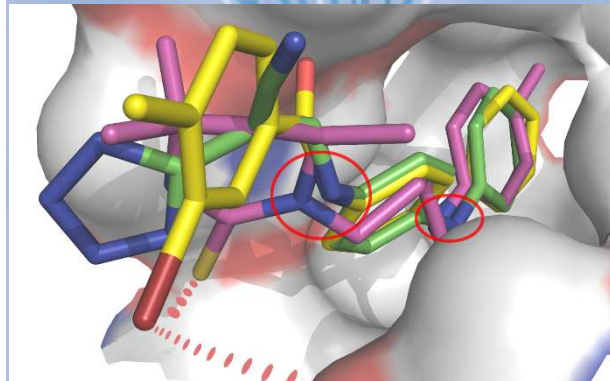


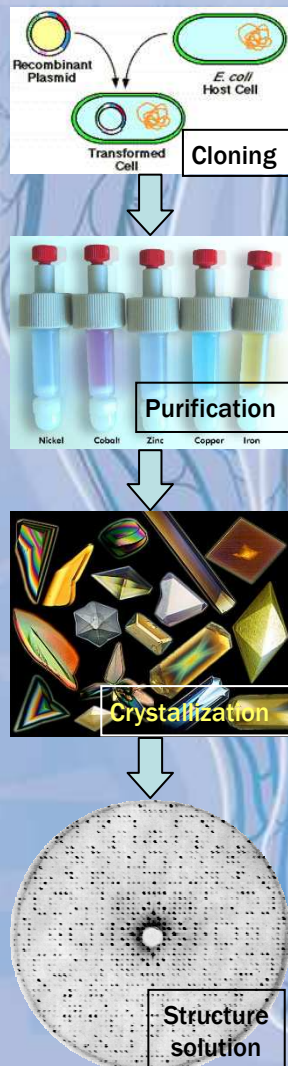
Molecular Bases of Disease

Building Bridges between Protein Structure and Pathophysiology



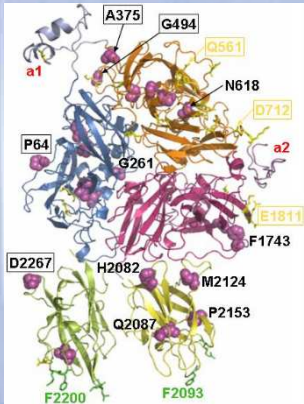
Our slogan: “Precision medicine means structure-based medicine.”

Structural Biology @Sant Pau - From Protein Expression to X-ray Crystallography

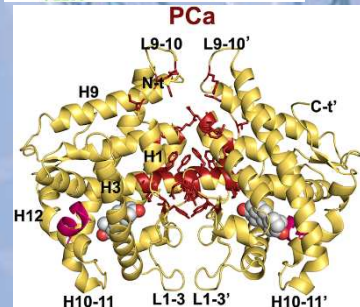


- Clone, overexpress, purify and characterize definite domains of human proteins of interest.
- Perform biochemical and biophysical experiments (from enzyme kinetics and Biacore to NMR and X-ray crystallography) to understand the function of these proteins. (**Structure-function investigations**).
- Use state-of-the-art knowledge and software to predict protein structures, impact of point mutations / SNVs, etc. (**Bioinformatics**).

Some Success Stories – From Hemophilia to Prostate Cancer



- Blood clotting and blood clotting disorders: Structural basis of factor V activation (Corral-Rodríguez *et al.*, Blood 2011), analysis of F8 mutants identified in hemophiliacs (e.g., Venceslá *et al.*, Blood 2008).



- Androgen receptor (AR) and prostate cancer: Resolution of the 3D structure of the active, dimeric conformation of AR hormone-binding domain (Nadal *et al.*, Nat Commun 2017). New avenues for antiandrogen design currently explored.

- Lipid metabolism: Structure-function analysis of APOA5 mutations found in patients with severe hypertriglyceridemia (Mendoza-Barberà *et al.*, J Lipid Res 2013); identification of LRP1 domain critical for internalizing agLDL (Costales *et al.*, JBC 2015).

What's Next: Current Projects, Challenges and Opportunities

- Neurodegenerative diseases:
 - Spinal Muscular Atrophy (SMA), structural basis of exon 7 skipping from *SMN2* transcripts (work in progress, Daniel Bravo grant).
 - structure of PINK1 and relevance for Parkinson's disease.
- Other cancer-related projects:
 - Structure-based classification of *TET2* mutations and SNVs; relevance for hematopoietic neoplasms (Bussaglia *et al.*, submitted).
 - Impact of common *LRIG1* SNPs on colorectal cancer treatment.

