Talin is associated with multiple diseases

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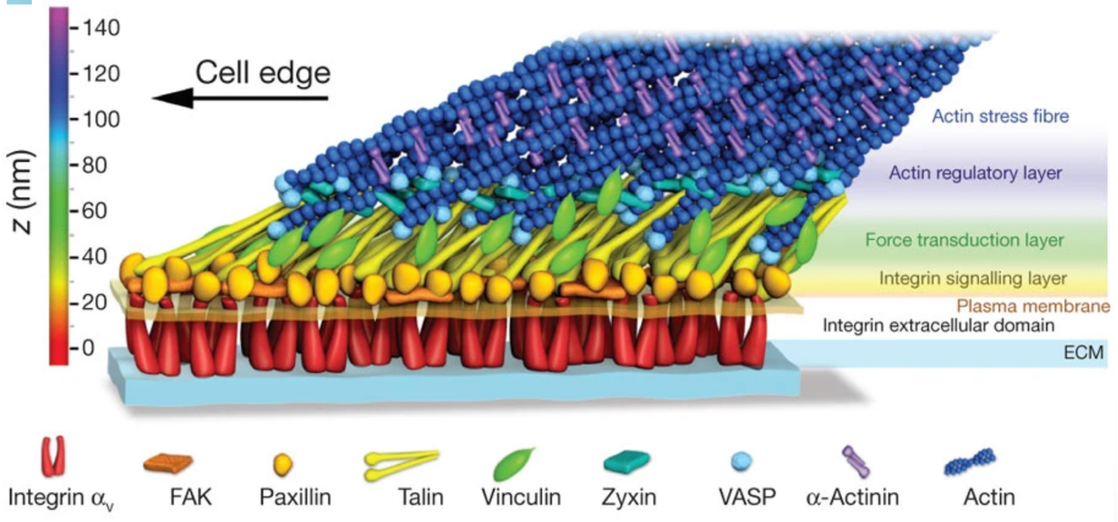
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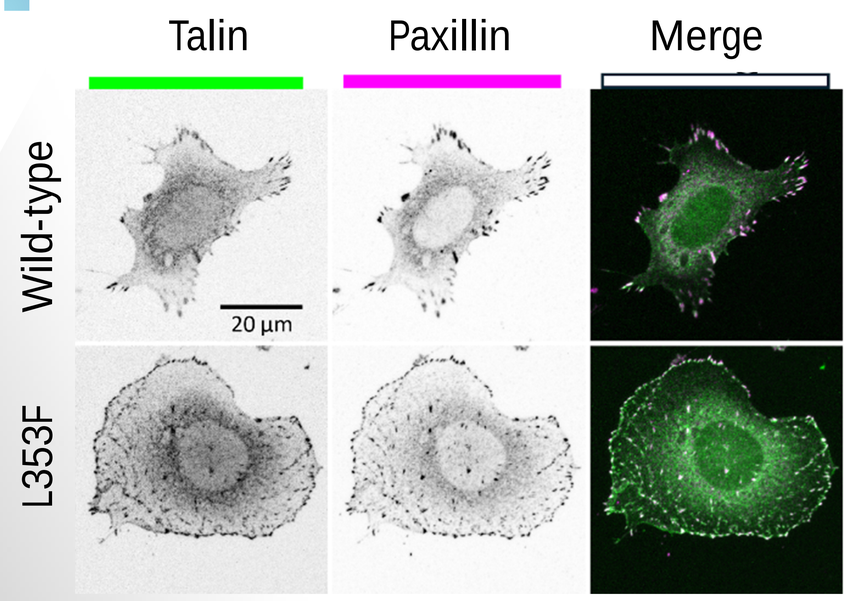
Talin is a large cytoplasmic adaptor protein that connects integrins to the actin cytoskeleton, enabling force transmission between cell and the extracellular matrix (1). This linkage is essential for processes such as cell spreading and polarization. Talin missense mutations are associated with cardiovascular defects (2) and altered blood cell composition (3,4). These disease-associated variants cause only subtle changes in talin structure and function, resulting in relatively mild cellular phenotypes (2-5). Overall, our data highlight talin as a central mechanosignaling hub whose mechanical integrity and force-regulated interactions are critical for cellular homeostasis (6). Given that such subtle mutations can produce diverse and complex phenotypes, we propose that additional, currently unrecognized talin-associated diseases exist, for which we suggest the term “talinopathies.”

Talin is a central component in cell-matrix interface

Kanchanawong et al. (2010) Nanoscale architecture of integrin-based cell adhesions. Nature 68:580



Talin mutation L353F influences focal adhesion composition



Clinical manifestations

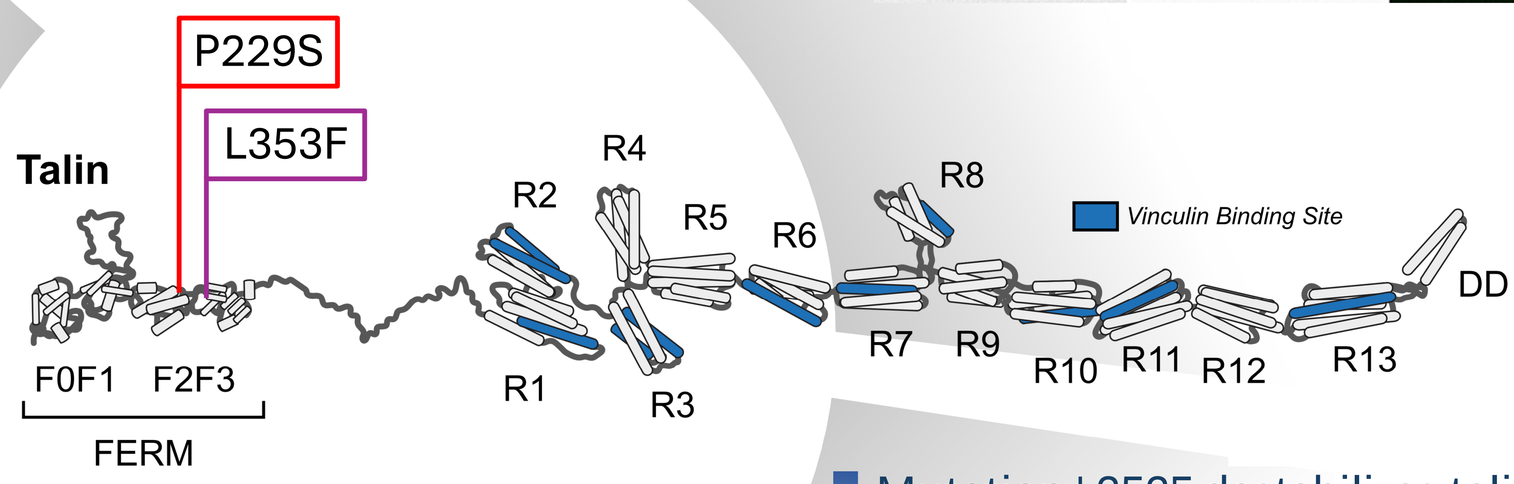


Clinical manifestations associated with P229S/L353F

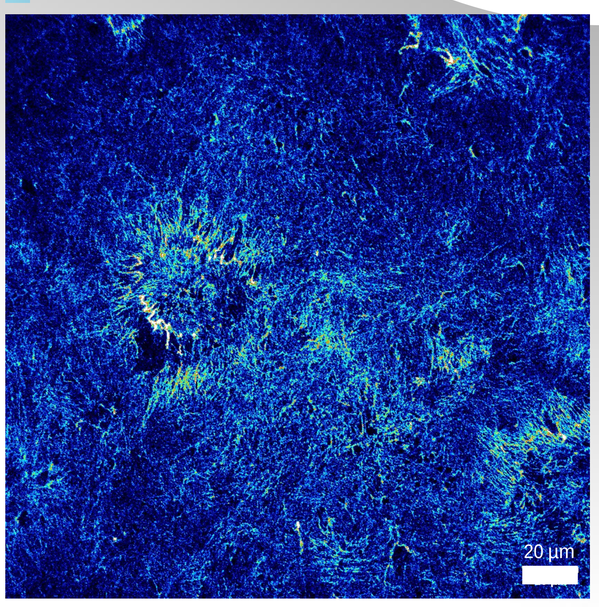
Skin related
- Eczematoid dermatitis (HP:0000964) ● ●
- Edema of the dorsum of hands (HP:0007514) ●
- Localized skin lesion (HP:0011355) ●
- Recurrent cutaneous fungal infections (HP:0011370) ●
- Keloid-like skin changes (HP:0001064) ●

Immune system related
- Thrombocytopenia (HP:0001873) ● ●
- Leukopenia (HP:0001882) ● ●
- Immunodeficiency (HP:0002721) ●
- IgG deficiency (HP:0004315) ●
- T lymphocytopenia (HP:0005403) ●
- Atypical common variable immunodeficiency ●

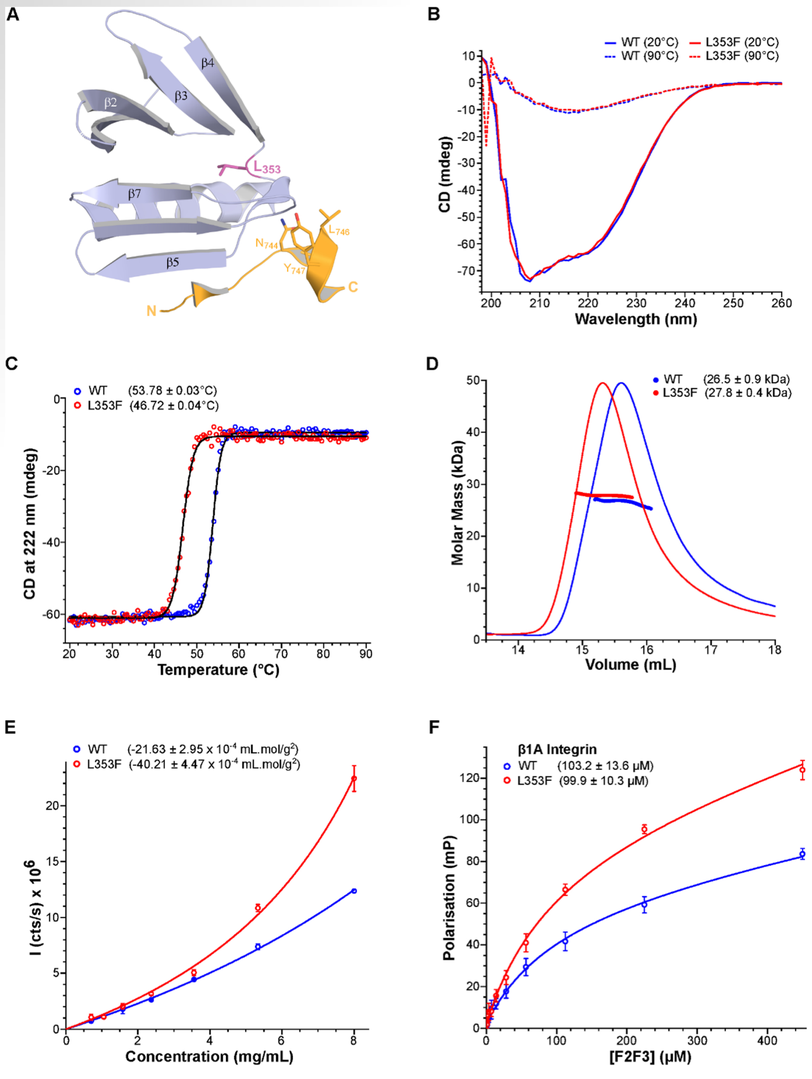
Other
- Congenital cataract (HP:0000519) ● ●
- Recurrent bronchitis (HP:0002837) ● ●
- Arthritis (HP:0001369) ●
- Arthralgia (HP:0002829) ●
- Hematuria (HP:0000790) ●
- Migraine (HP:0002076) ●
- Intestinal lymphangiectasia (HP:0002593) ●
- Tick-like body jerking ●
- Hearing impairment (HP:0000365) ●
- Elevated circulating hepatic transaminase concentration (HP:0002910) ●
- Recurrent sinusitis (HP:0000437) ●
- Recurrent otitis media (HP:0000403) ●



Matrix remodeling



Mutation L353F destabilizes talin but doesn’t affect integrin binding



Literature

1. Bachmann et al. (2019) Cell adhesion by integrins. Physiol. Rev. 99:1655-1699.
2. Azizi et al. (2024) Talin-1 variants associated with spontaneous coronary artery dissection (SCAD) highlight how even subtle changes in multi-functional scaffold proteins can manifest in disease. Hum. Mol. Genet. 33:1846.
3. Athale et al. (2025) De novo talin-1 variant L353F connects multifaceted clinical symptoms to alterations in talin-1 function. Biochem. J. 482:1337
4. Azizi et al. (2022) Talin variant P229S compromises integrin activation and associates with multifaceted clinical symptoms. Hum. Mol. Genet. 31:4159
5. Azizi et al. (2021) Cancer associated talin point mutations disorganise cell adhesion and migration. Sci. Rep. 11:347
6. Goult et al. (2022) The mechanical cell - the role of force dependencies in synchronising protein interaction networks. J. Cell. Sci. 135:jcs259769.

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