

Supplementary Online Data

Recessive *NUP54* variants underlie early-onset dystonia with striatal lesions

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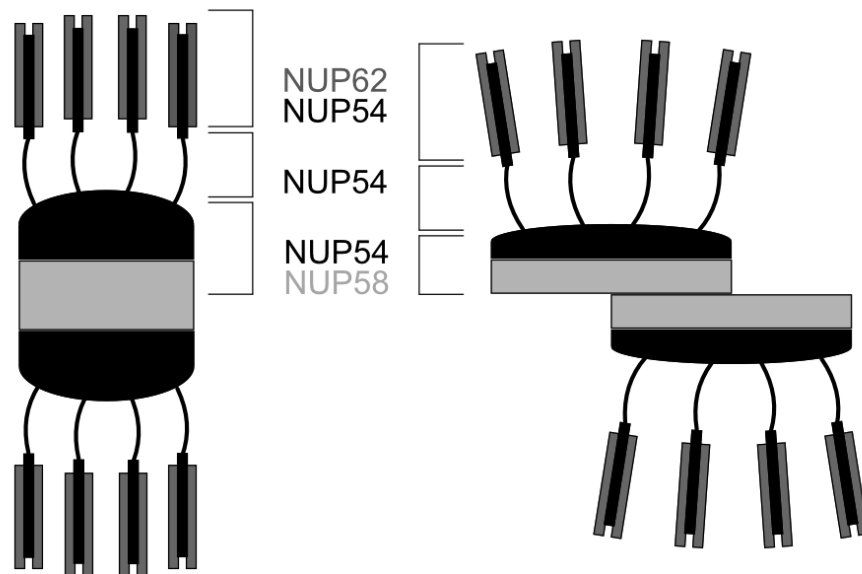
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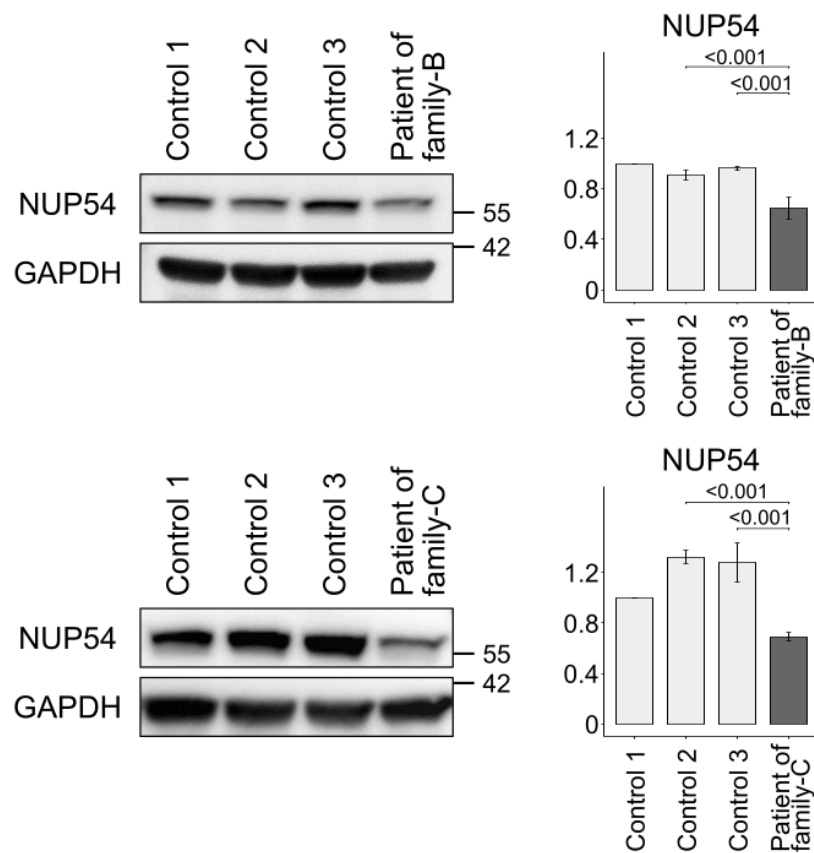
Supplementary Online Figure 1 NUP54 plays a key role in structural stabilization of the central transport channel of the nuclear-pore complex



Schematic diagram adapted from Sharma et al., 2015¹. Within the central channel of the nuclear-pore complex formed by NUP54, NUP62, and NUP58, NUP54 has a crucial function in providing plasticity to various multimerization processes. More specifically, the C-terminal coiled-coil regions of NUP54 form modular assemblies with the coiled-coils of NUP62 ("NUP54-NUP62 interactome") and NUP58 ("NUP54-NUP58 interactome"), which in turn are critically required to build "finger" (NUP54-NUP62) and "ring" (NUP54-NUP58) structures that organize the transport channel of the nuclear-pore complex. Hence, mutational changes of the coiled-coil motifs of NUP54 may deleteriously affect protein-protein interactions, thereby impairing the protein's ability to maintain structurally important assemblies with NUP62/NUP58 within the nuclear-pore complex.

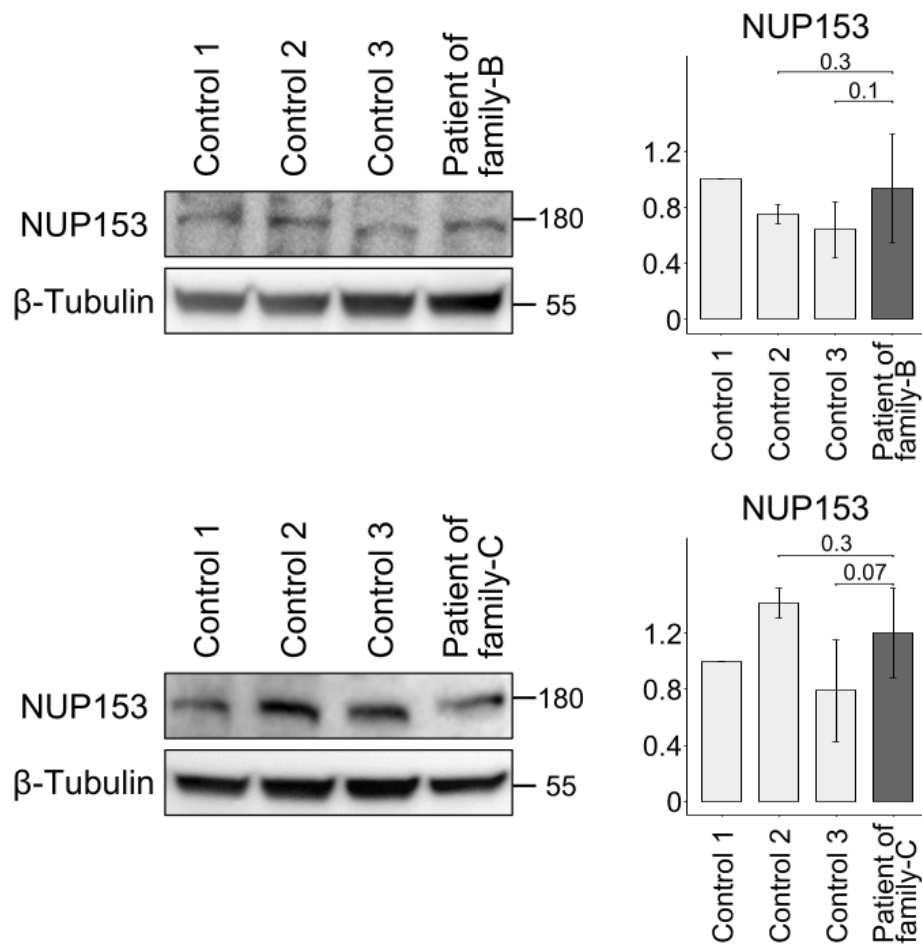
1. Sharma A, Solmaz SR, Blobel G, Melcak I. Ordered Regions of Channel Nucleoporins Nup62, Nup54, and Nup58 Form Dynamic Complexes in Solution. J Biol Chem. 2015 Jul 24;290(30):18370-8.

Supplementary Online Figure 2 Confirmation of reduced NUP54 protein levels in patient fibroblasts by use of an independent antibody



NUP54 protein levels were detected in patient fibroblasts (families B and C) by use of the NUP54-specific antibody HPA035929 (SIGMA-ALDRICH). Consistent with the data obtained in western-blot studies with the NUP54-directed antibody ab220890 (abcam; Figure 2B), a significantly decreased abundance of NUP54 was seen.

Supplementary Online Figure 3 Normal levels of the non-channel-related nuclear-pore complex component NUP153 in patient fibroblasts



NUP153 protein levels were unaltered in patient fibroblasts (families B and C) as compared to controls, confirming a specific decrease in channel-NUPs in relation to the *NUP54* variants identified in this study.

Video Legends

Video S1: This clip demonstrates severe dystonic symptoms in the patient of family-A at last examination (age 22 years): dystonia affects the upper limbs bilaterally with strongly impaired motor performance, the trunk, and the cranio-cervical district with latero- and retrocollis; note massive involvement of the oro-bulbar region with dysarthria, dysphagia, and drooling. The patient uses preferentially a wheelchair but is able to walk short distances (see next clip Video S2).

Video S2: This clip demonstrates gait impairment in the patient of family-A at last examination (age 22 years): generalized dystonia with bilateral lower limb dystonic postures resulting in significant gait instability; an ataxic component is also seen.