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Supplemental Data

Missense Mutations in the Copper Transporter Gene

ATP7A Cause X-Linked Distal Hereditary Motor Neuropathy

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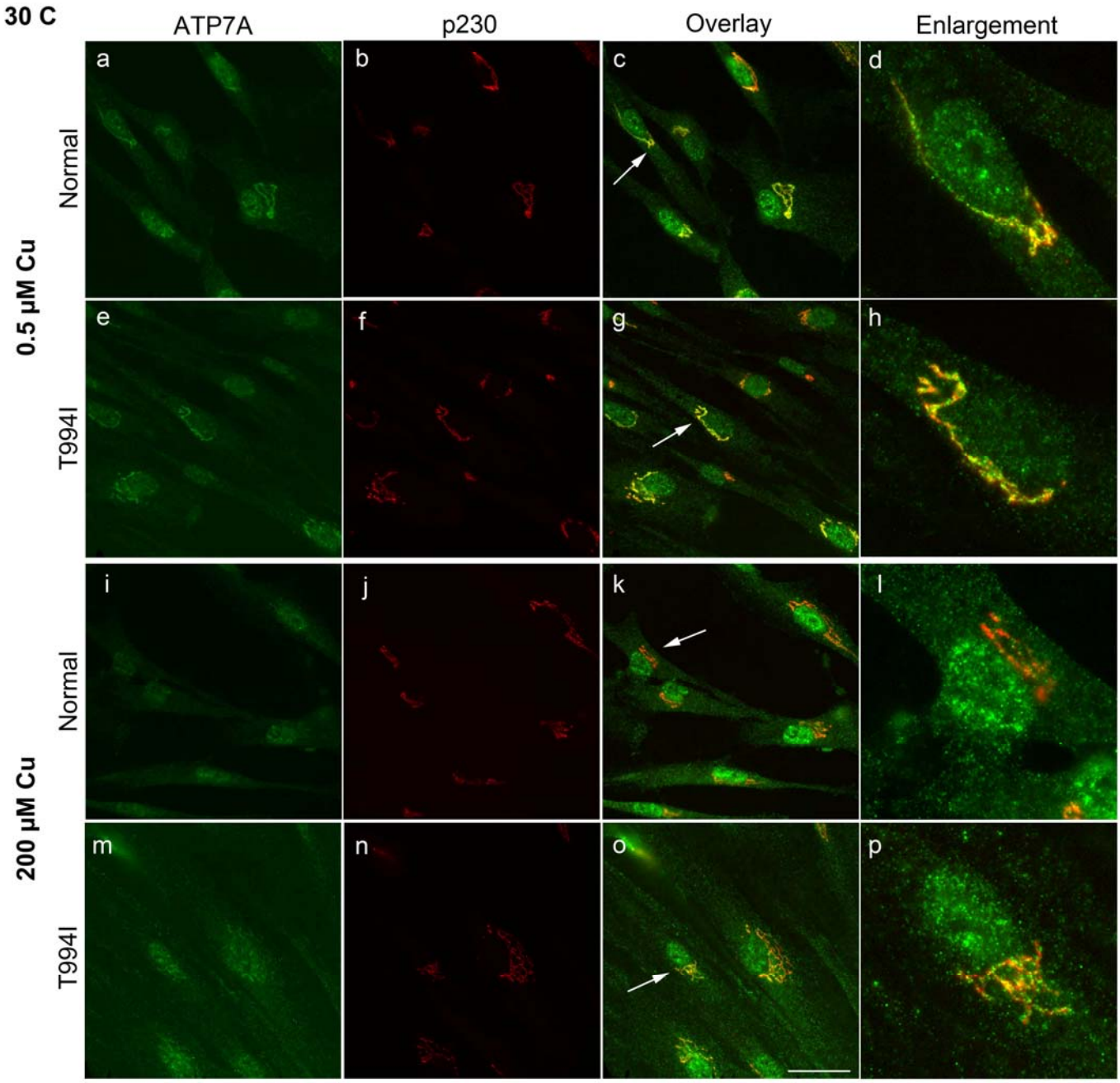
Figure S1. Effect of temperature and copper concentration on the intracellular localization of ATP7A at 30°C in cultured T994I fibroblasts.



In 0.5μM copper, both wild type (panel a and c) and T994I mutant (panel e and g) ATP7A (green in these panels) show extensive co-localization with the p230 *trans* Golgi marker (red in panel b and f) overlay in panel c and g. In 200μM copper, the wild type ATP7A shows trafficking out of the *trans* Golgi (i) with minimal co-localization with p230 (overlay in k). In contrast, the mutant T994I ATP7A shows retention in the *trans* Golgi (panel m) and extensive perinuclear yellow remains indicating co-localization with the p230 marker (panel o). To further demonstrate the difference in trafficking, cells indicated by the white arrows were enlarged and are shown in panels d, h l and p. Panels d and h clearly show the extensive areas of co-localization of both the wild type and T994I ATP7A in 0.5 μM copper. Panel l shows the complete trafficking of ATP7A from the *trans* Golgi leaving only red staining of p230 in the *trans* Golgi. Panel p shows extensive areas of yellow indicating much of the mutant ATP7A remains in the *trans* Golgi. Photographs were taken using a 63X objective with a Leica TCS SP2 confocal microscope (scale bar is 40 μm).