Supporting Information

Zinc promotes liquid–liquid phase separation of tau protein

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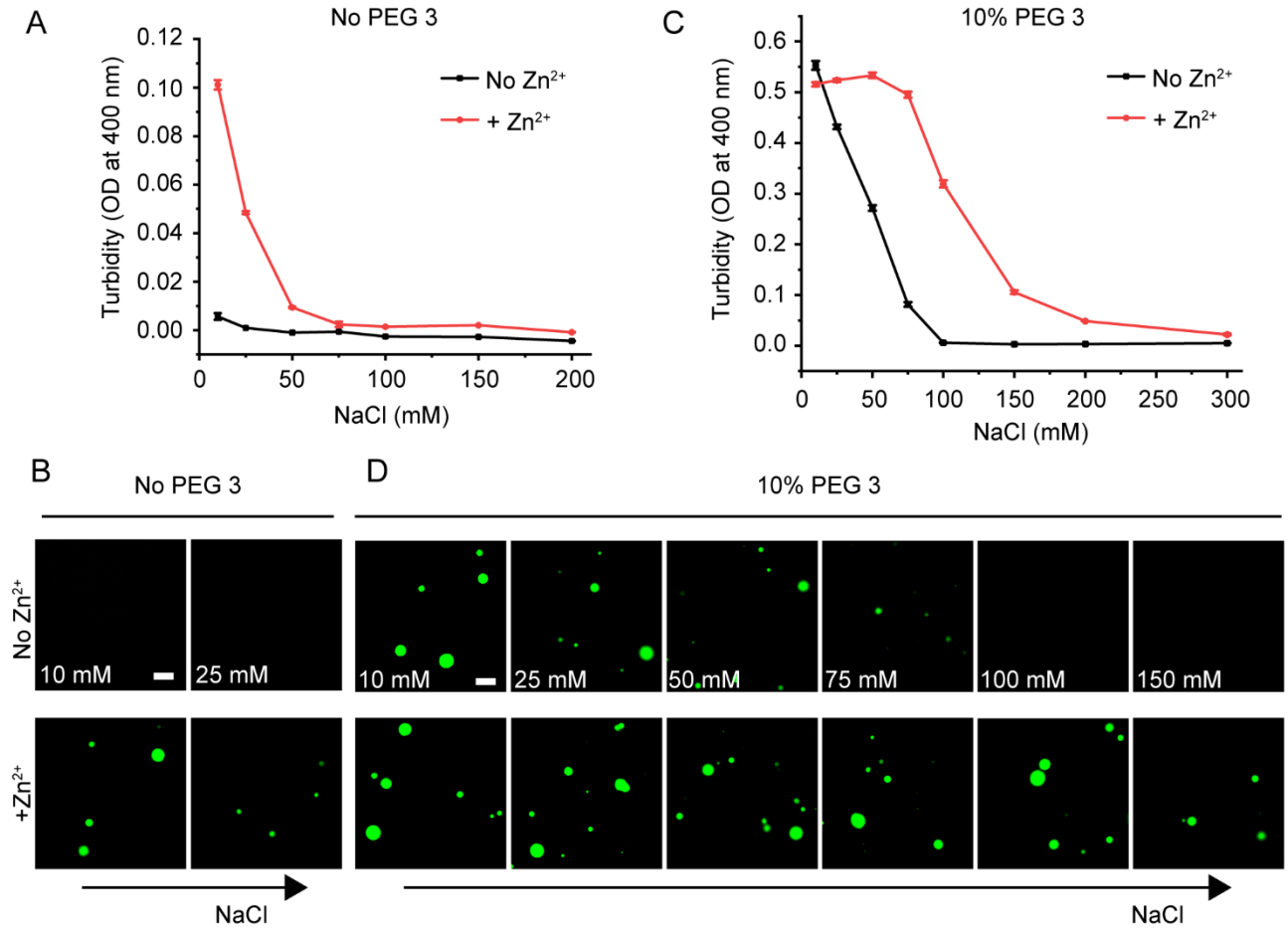

Figure S1. The effect of ionic strength on Zn^{2+}-induced tau441 LLPS in the absence and presence of a crowding agent. *A*, Turbidity of tau441 (10 µM) in PEG 3-free buffer as a function of ionic strength in the absence (black) and presence of 40 µM zinc (red). Error bars represent S.D. (n = 5). *B*, Representative fluorescence microscopy images of tau441 (10 µM) in PEG 3-free buffer in the absence (top panels) and presence of 40 µM Zn^{2+} (bottom panels).as a function of ionic strength. The numbers labeling top panels indicate concentration of NaCl. These numbers apply also to bottom panels. Scale bar: 5 µm. *C*, Turbidity of tau441 (10 µM) in a buffer containing 10% PEG 3 as a function of ionic strength in the absence (black) and presence of 40 µM zinc (red). Error bars represent S.D. (n = 5). *D*, Representative fluorescence microscopy images of tau441 (10 µM) in a buffer containing 10% PEG 3 in the absence (top panels) and presence of 40 µM Zn^{2+} (bottom panels). Scale bar: 5 µm. The numbers labeling top panels indicate concentration of NaCl. These numbers apply also to bottom panels. The image shown in the fifth bottom panel is identical to that shown in the right bottom panel of Fig. 1B; both of these panels represent data in a buffer containing 10% PEG 3, 100 mM NaCl and 40 µM Zn^{2+}.

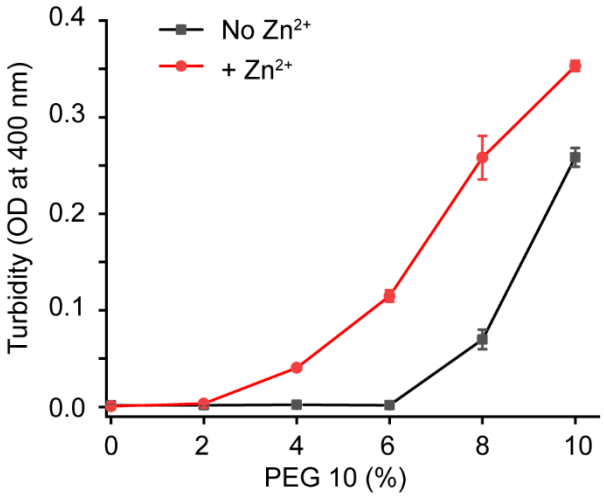

Figure S2. The effect of 10-kDa PEG (PEG 10) on tau441 LLPS in the absence and presence of zinc. Turbidity (OD at 400 nm) of tau441 (10 µM) in the absence (black) and presence of 40 µM Zn^{2+} (red). Experiments were performed in 10 mM HEPES buffer (pH 7.4) containing 100 mM NaCl. Error bars represent S.D. (n = 5).

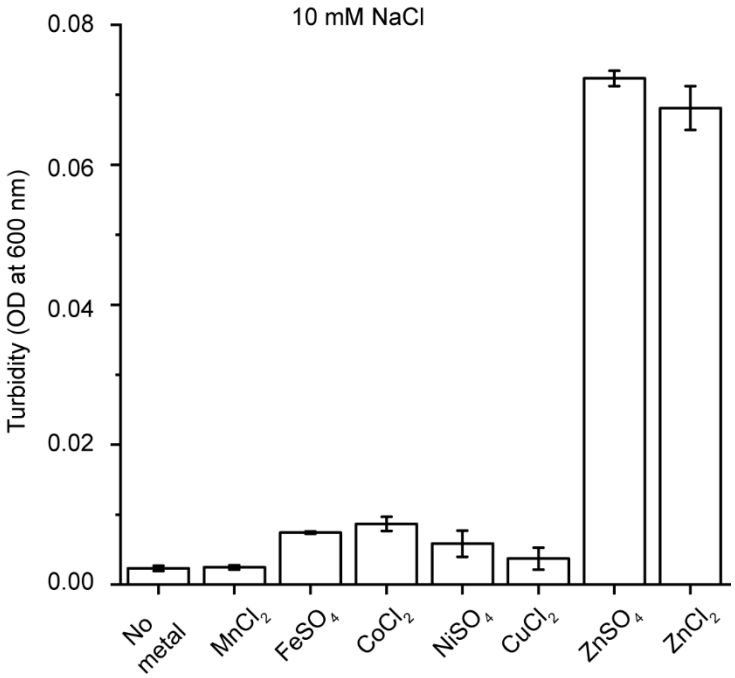

Figure S3. Zinc-specific promotion of tau441 LLPS in low ionic strength buffer. Turbidity (OD at 600 nm) of tau441 (10 µM) in the presence of different transition metal salts (40 µM each) in 10 mM HEPES buffer (pH 7.4) containing 10 mM NaCl and no crowding agent. Error bars represent S.D. (n = 5).

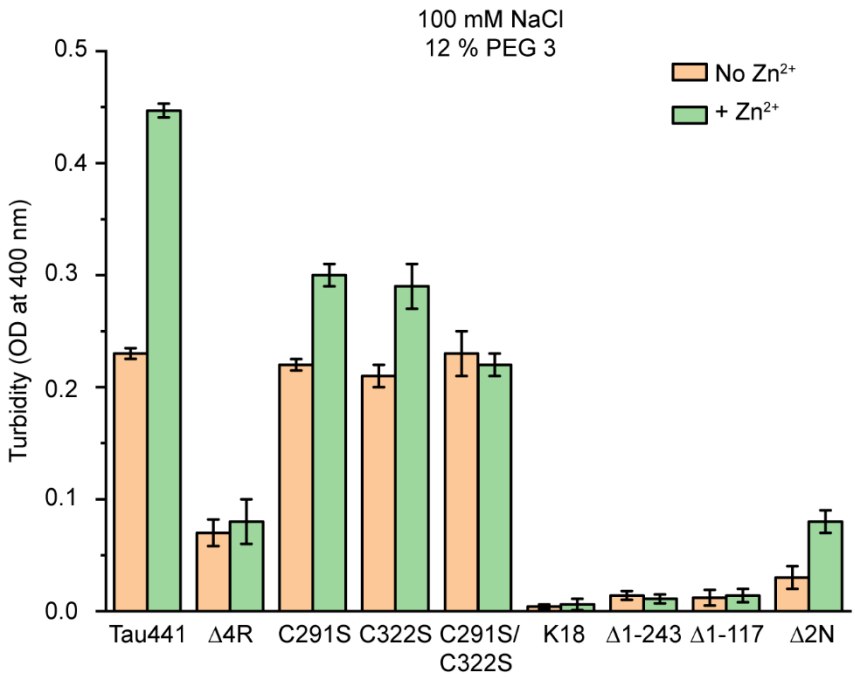

Figure S4. The effect of zinc on LLPS of individual deletion/substitution variants of tau441 in high ionic strength buffer in the presence of 12% PEG 3. Turbidity (OD at 400 nm) of different tau variants (10 µM each) in 10 mM HEPES buffer (pH 7.4) containing 100 mM NaCl and 12% PEG 3 in the absence (orange) and presence (green) of 40 µM Zn^{2+}. Error bars represent S.D. (n = 5).