Nucleophosmin integrates within the nucleolus via multi-modal interactions with proteins displaying R-rich linear motifs and rRNA

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Figure 1. Multivalency of acidic tracts within NPM1 and R-motifs within nucleolar substrates mediates liquid-liquid phase separation. (a) Composite model of NPM1 structure; the oligomerization domain (OD, green, PDB ID 4N8M), containing the A1 acidic tract (red), is connected via a disordered region (IDR, grey), containing two additional acidic tracts (A2 & A3, red), to the C-terminal nucleic acid binding domain (NBD, blue, PDB ID 2VXD); (b) Phase separation diagrams for mixtures of N130 and four R-motif containing peptides (bottom dot graphs); phase separation was assessed by the formation of liquid-like droplets detected using light microscopy (grey dot, clear solution observed; green dot, liquid-like droplets observed). Representative examples of liquid-like droplets formed between 50 µM N130 and the lowest peptide concentration associated with phase separation, visualized by DIC (top panel) and Alexa Fluor488 emission of labeled N130 (bottom panel) are illustrated. The composition of the R-motif peptides is given at the top of each pair of images; R is arginine; and X is any other amino acid.

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