**Supp. Fig. Legends**

**Supp. Fig. 1.** The eIF4E sensitivity element (4ESE) associates with specific protein factors as determined by RNA pull down assay and mass spectrometry. **A.** Left panel: Representative gel of the pulled-down proteins, visualized by Sypro Ruby, using uncapped and non-polyadenylated LacZ and LacZ4E-SE RNA baits (see method section). Here, we used the 4ESE from cyclin D1 (c4E-SE). Differences in band patterns between the material pulled down with LacZ or LacZ-4ESE indicate we can isolate proteins specifically bound to 4ESE by using this approach. Black arrows indicate specific bands; red arrow indicates the position of LRPPRC. Right panel: Comparative analysis of proteins pulled down by 4ESE RNA from Cyclin D1 (c4E-SE) and Pim-1 (p4E-SE). Gel illustrates a highly similar profile for proteins pulled down by each 4ESE. **B. Cellular fractionation.** U2Os cells were fractionated into post-TX, TX-100 and digitonin fraction and the amount of indicated proteins in each fraction was determined by western blot. **C. eIF4E does not associate with non-shuttling hnRNP C1/C2.** Immunoprecipitations were carried out in U2Os cells using anti-eIF4E (IP-4E), anti-hnRNP C1/C2 (IP-C1/C2) antibody, or with the control IgG (IP-IgGm). Immunoprecipitated material was analysed by western blot using the indicated antibodies.

**Supp. Fig. 2.** LRPPRC contains putative eIF4E binding sites. LRPPRC contains putative eIF4E binding sites. **A.** Primary sequence of human LRPPRC (gi:31621305) residues 421-720. Underline in red, are three putative eIF4E recognition motifs. Above the sequence is a cartoon representation of helices predicted by PredictProtein software (http://www.predictprotein.org). Structural and biophysical studies show that the eIF4E recognition motif forms a short α-helical conformation when it interacts with the dorsal surface of eIF4E (Gross et al., 2003). Other known eIF4E binding proteins contain similar recognition motifs. **B.** Sequence alignment of the
putative 4E binding sites in human LRP with sequences from known eIF4E interacting proteins.


**Supp. Fig. 3.** LRPPRC overexpression does not affect total levels of eIF4E sensitive mRNAs. A. U2Os cells were transfected with an empty vector, wild-type LRPPRC (LRP), or Y441A LRPPRC mutant (Y441A). B. U2Os cells were treated with the negative control (DS) or LRP siRNA (siLRP). In both cases, total transcripts levels were determined using RT-qPCR. Bar graphs represent mean values ± SD (n=3). C. Fractionation controls for the cells transfected or treated as indicated are given Relative abundance of the nuclear (U6snRNA) and cytoplasmic (tRNA<sub>Lys</sub>) RNA marker was determined using sqRT-PCR. n-nuclear; c-cytoplasmic fraction. Asterisk indicates the non-specific PCR product. D. U2Os cells stably expressing Xpress tagged LacZ and LacZ-4E-SE were transfected with vector, wild-type LRPPRC (LRP), or Y441A LRPPRC mutant. E. U2Os cells expressing the LacZ fusions were treated with the negative control (DS) or with LRP siRNA (siLRP). In both cases, transcript levels were determined using RT-qPCR. Bar graphs represent mean values ± SD (n=3). F. These cells were fractionated into nuclear (n) and cytoplasmic (c) fraction. Relative abundance of the nuclear (U6snRNA) and cytoplasmic (tRNA<sub>Lys</sub>) RNA marker was determined using sqRT-PCR.

**Supp. Fig. 4.** Effects of the RNAi knockdown of endogenous LRPPRC levels can be efficiently rescued by the overexpression of the wildtype LRPPRC, but not with Y441A
Mutant. Mutations on the dorsal surface of eIF4E affect its nucleocytoplasmic trafficking.

A. U2Os or U2Os/LacZ-4E-SE cells (U2Os/4ESE) were treated with lipofectamine (Lipo), negative control (DS), LRP siRNA targeting the coding region and used throughout this study (siLRP) or with LRP siRNA targeting the 3’UTR region (siLRPUTR). In the latter case upon siRNA treatment cells were transfected with myc-tagged wild type LRPPRC or LRPPRC Y441A mutant both lacking the 3’UTR region targeted by siLRPUTR. Upon the treatment cells were lysed and the levels of indicated proteins were determined by western blot using appropriate antibodies (W.B.). α-tubulin served as a loading control. B. U2Os cells were transfected with an empty vector or with indicated Xpress-tagged eIF4E constructs. Upon transfection cells were fractionated into nuclear and cytoplasmic fraction and the distribution of wild type and mutant eIF4E protein was monitored by western blot (W.B.) using anti-Xpress antibody. α-tubulin and SC35 were used as cytoplasmic and nuclear marker, respectively. C. U2Os cells were transfected with an empty vector, myc-tagged eIF4E wild type (WT) or with indicated myc-tagged eIF4E constructs containing heterologous NLS (+NLS). Experiments were carried out as in B.

Supp. Fig. 5. LRPPRC and eIF4E are exported from nucleus in a CRM-1 dependent fashion. U2Os cells were treated for 4 hours with either 50 nM Leptomycin B (+LMB) or with the appropriate amount of the vehicle (ethanol; -LMB). A. Representative confocal micrographs showing the subcellular distribution of LRPPRC (LRP) or eIF4E (4E) (both in green) as a function of LMB treatment. Nuclei were counterstained with DAPI (blue). Overlays of the green and blue channel are shown on the right. B. Same cells were fractionated into the nuclear (n) and cytoplasmic (c) fraction and the subcellular distribution of LRPPRC (LRP) and eIF4E was analysed by western blot. α-tubulin and hnRNPC1/C2 were used as cytoplasmic and nuclear marker, respectively.
Supp. Fig. 6. LRPPRC affects the subcellular localization of eIF4E. U20s cells were transfected with an empty vector, Y441A LRPPRC mutant (Y441A), wild-type LRPPRC (LRP), negative control (DS) or LRP siRNA (siLRP). A. Representative confocal micrographs showing the subcellular distribution of LRPPRC (LRP; red) or eIF4E (green) in the indicated cells. Nuclei were counterstained with DAPI (blue). Overlays of all three channels are shown on the right. Green arrowheads point to cytoplasmic eIF4E speckles, formation of which was induced by the knockdown of LRPPRC levels B. U2Os cells were transfected as in A. (Left panel) Expression of LRPPRC upon the transfections was verified by western blot. α-tubulin was used as a loading control. (Right panel) Same cells were fractionated and the subcellular distribution of eIF4E in was determined by western blot. α-tubulin and hnRNPC1/C2 were used as cytoplasmic (c) and nuclear (n) marker, respectively.

Supp. Figure 1.
Supp. Fig. 3
Supp. Fig. 4
Supp. Fig. 5