Supplemental Figure S1

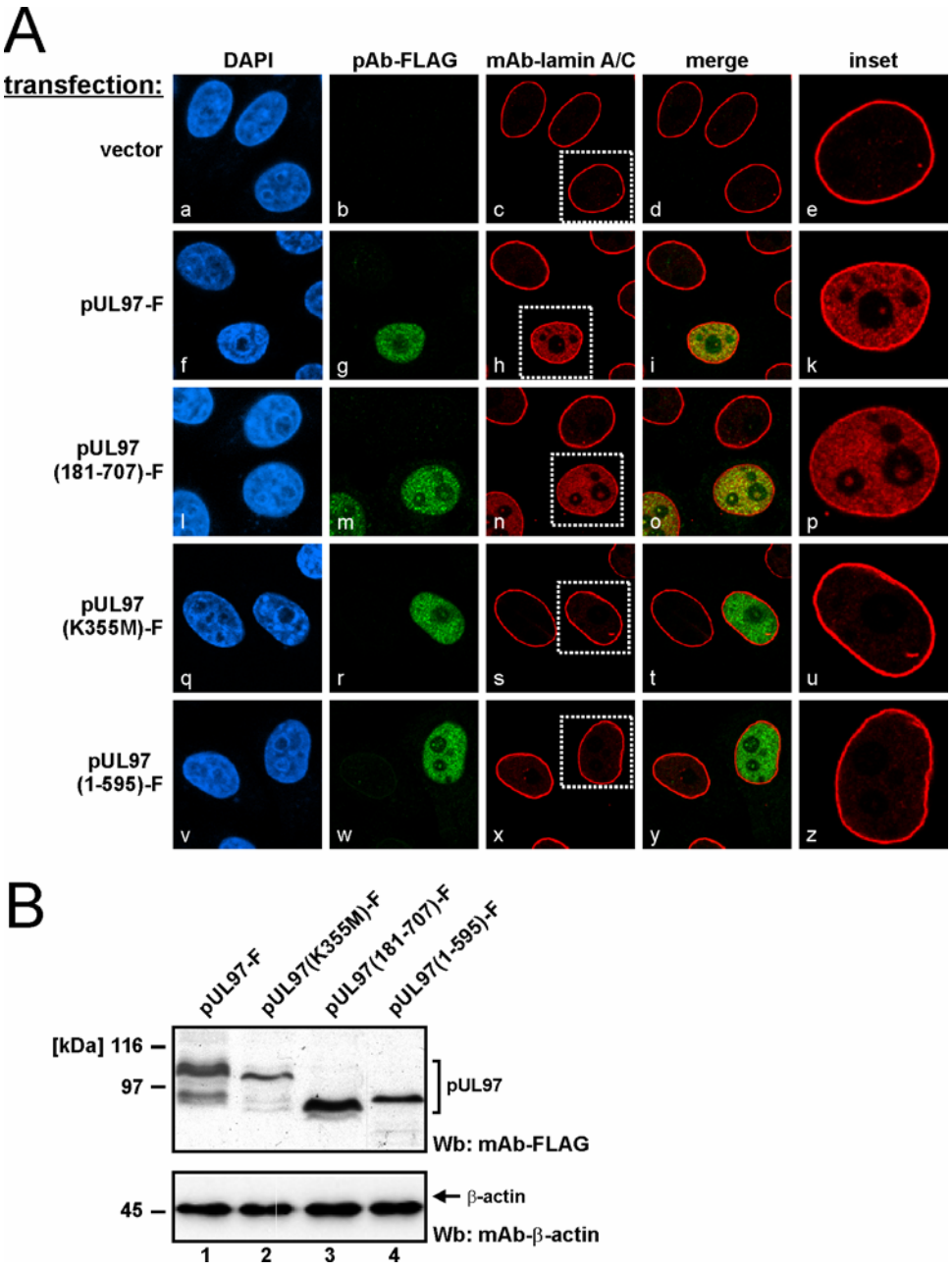

Fig. S1. Morphological alteration of the nuclear lamina induced by pUL97. HeLa cells (A) or 293T cells (B) were transfected with constructs expressing catalytically active or inactive mutants of pUL97. (A) Confocal laser-scanning microscopy. At 2 days post-transfection, cells were fixed and coimmunostained with pAb-FLAG and mAb-lamin A/C (using FITC- or Cy3-conjugated secondary antibodies, respectively). Cell nuclei were counterstained with DAPI (panels a, f, l, q and v). Inset images (panels e, k, p, u and z) show enlarged nuclei of cells expressing kinase-active (panels f-p) or kinase-inactive (panels q-z) pUL97, respectively. (B) Expression levels of pUL97 mutants. At 2 days post-transfection, cells were lysed and subjected to semi-quantitative Wb analysis using mAb-FLAG or mAb-β-actin.

Supplemental Figure S2

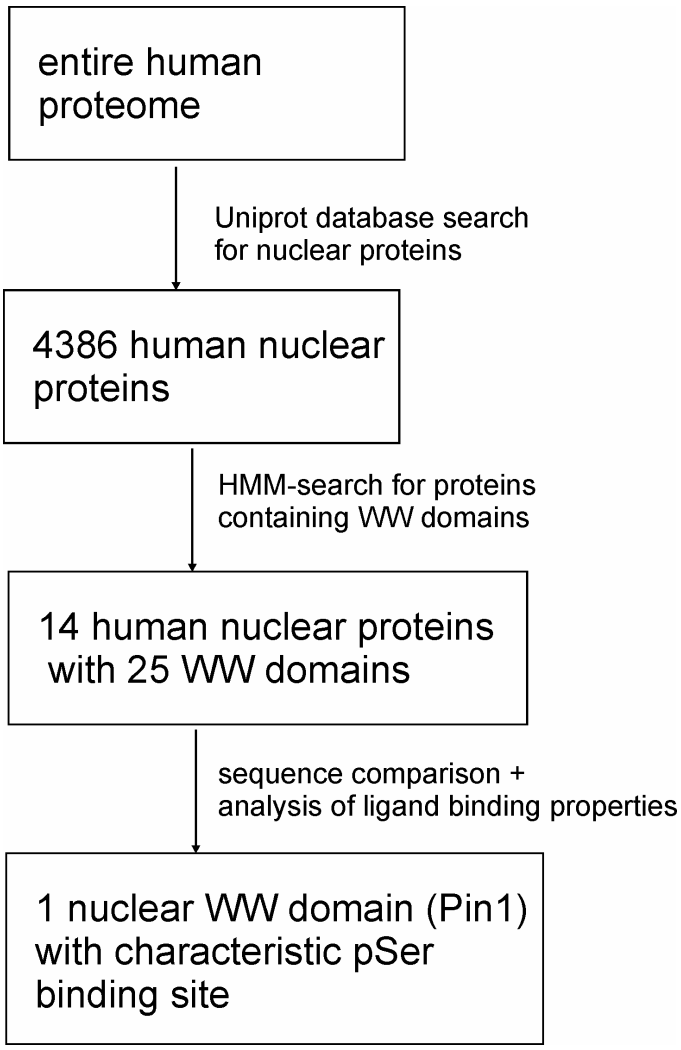

Fig. S2. Flowchart for the prediction of interaction partners of the phosphorylated lamins (see text for details).

Supplemental Figure S3

E-value	score	N	Sequence	Description
4.6e-49	172.7	4	ITCH_HUMAN	E3 ubiquitin-protein ligase Itchy homolog
2e-31	116.4	3	SMUF2_HUMAN	E3 ubiquitin-protein ligase SMURF2
9e-23	88.7	3	TCRG1_HUMAN	Transcription elongation regulator 1
4e-20	80.2	2	PR40A_HUMAN	Pre-mRNA-processing factor 40 homolog
4.5e-17	70.5	2	WWOX_HUMAN	WW domain-containing oxidoreductase
1.2e-16	69.1	2	WBP4_HUMAN	WW domain-binding protein 4
1.7e-16	68.6	2	PR40B_HUMAN	Pre-mRNA-processing factor 40 homolog
4.2e-13	57.8	1	PIN1_HUMAN	Peptidyl-prolyl cis-trans isomerase
6.3e-13	57.2	1	MAGI3_HUMAN	Membrane-associated guanylate kinase
3.7e-08	42.0	1	WWTR1_HUMAN	transcription regulator protein 1
6.7e-07	37.9	1	SETD2_HUMAN	Histone-lysine N-methyltransferase
3.4e-06	35.7	1	APBB1_HUMAN	Amyloid beta A4 precursor protein-binding
7.6e-06	34.6	1	WAC_HUMAN	WW domain-containing adapter protein
1.3e-05	33.8	1	PQBP1_HUMAN	Polyglutamine-binding protein 1

Fig. S3. List of the human nuclear proteins containing at least one WW domain. The hits were obtained from a HMM search as described in methods. The E values and score of the hit are given in the first two columns. N denotes the number of WW domains present in each hit. The UniProt Sequence Identifier and a short description are given for each hit.

Supplemental Figure S4

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ITCH_HUMAN/328-357       ---LPPGWEQRVD-QHGRVYYVDHVEKRTTWDRP
ITCH_HUMAN/360-389       ---LPPGWERRVD-NMGRIYYVDHFTRTTTWQRP
ITCH_HUMAN/440-469       ---LPPGWEKRTD-SNGRVYFVNHNTRITQWEDP
ITCH_HUMAN/480-509       ---LPEGWEMRFT-VDGIPYFVDHNRRTTTYIDP
SMUF2_HUMAN/159-188      ---LPDGWEERRT-ASGRIQYLNHITRTTQWERP
SMUF2_HUMAN/253-282      ---LPEGYEQRTT-QQGQVYFLHTQTGVSTWHDP
SMUF2_HUMAN/299-328      ---LPPGWEIRNT-ATGRVYFVDHNNRTTQFTDP
TCRG1_HUMAN/134-162      -ee---IWVENKT-PDGKVYYYNARTRESAWTKP
TCRG1_HUMAN/432-460      --v--SEWTEYKT-ADGKTYYYNNRTLESTWEKP
TCRG1_HUMAN/530-559      -pg--TPWCVVWT-GDERVFFYNPTTRLSMWDRP
PR40A_HUMAN/142-171      --a-KSMWTEHKS-PDGRTYYYNTETKQSTWEKP
PR40A_HUMAN/183-212      ---SKCPWKEYKS-DSGKPYYYNSQTKESRWAKP
WWOX_HUMAN/18-47         ---LPPGWEERTT-KDGWVYYANHTEEKTQWEHP
WWOX_HUMAN/59-88         ---LPYGWEQETD-ENGQVFFVDHINKRTTYLDP
WBP4_HUMAN/124-153       --s-KGRWVEGIT-SEGYHYYYDLISGASQWEKP
WBP4_HUMAN/165-194       vkt---VWVEGLS-EDGFTYYYNTETGESRWEKP
PR40B_HUMAN/95-123       ral----WSEHVA-PDGRIYYYNADDKQSVWEKP
PR40B_HUMAN/135-164      --s-QCPWKEYKS-DTGKPYYYNNQSKESRWTRP
PIN1_HUMAN/7-37          ---LPPGWEKRMSRSSGRVYYFNHITNASQWERP
MAGI3_HUMAN/295-324      ---LPKNWEMAYT-DTGMIYFIDHNTKTTTWLDP
WWTR1_HUMAN/126-155      ---LPPGWEMTFT-ATGQRYFLNHIEKITTWQDP
SETD2_HUMAN/2391-2420    ---LPPNWKTARD-PEGKIYYYHVITRQTQWDPP
APBB1_HUMAN/255-283      ---LPAGWMRVQD-TSG-TYYWHIPTGTTQWEPP
WAC_HUMAN/131-160        sad---DWSEHIS-SSGKKYYYNCRTEVSQWEKP
PQBP1_HUMAN/48-78        ---LPPSWYKVFDPSCGLPYYWNADTDLVSWLSP
```

Fig. S4. Multiple sequence alignment of the WW domains detected by the sequence search shown in Fig. S3. For each protein, the UniProt Sequence Identifier and the sequence position of the respective WW domain is listed. The key arginine in Pin1 required for the recognition of phosphorylated ligands is highlighted in bold. WW domains, for which experimentally determined complex structures are available, are marked in blue and their structural analysis is shown in Fig. S4.

Supplemental Figure S5

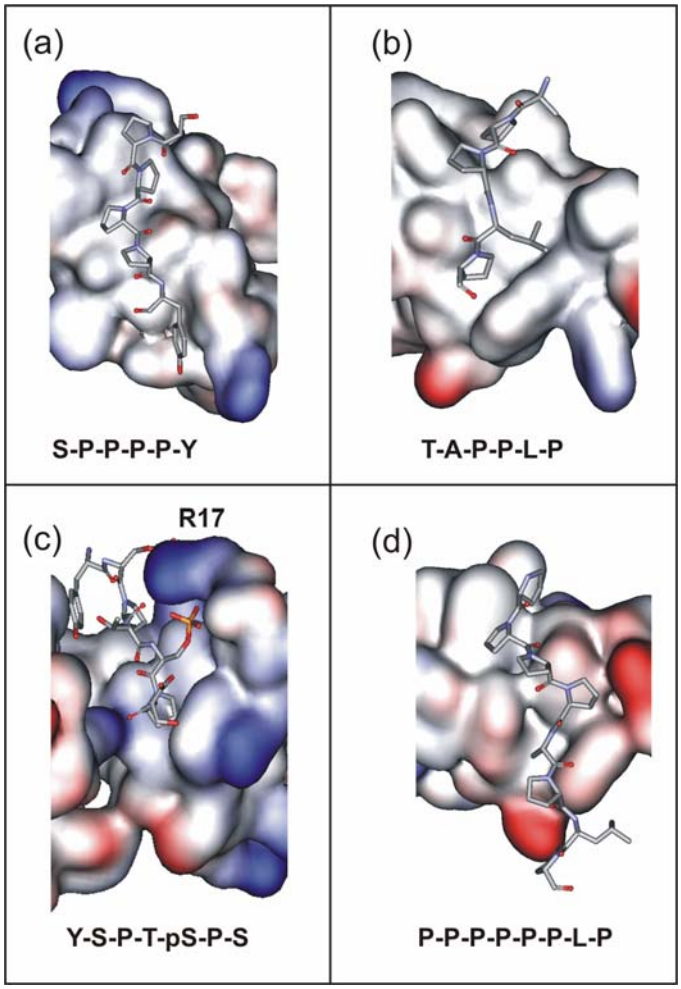

Fig. S5. Structure and ligand binding properties of several nuclear human WW domains. The experimentally determined complex structures of the WW domains from ICHT_HUMAN (a), PR40A_HUMAN (b), PIN1_HUMAN (c), and APBB1_HUMAN (d) are shown. WW domains are shown in space-filled presentation and are colored according to their charge. Ligands are shown in stick presentation, and their sequence is given below the structure. Note the presence of a unique arginine (R17) in Pin1 which has no equivalent in the other WW domains.