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Supplemental Information

Class I HDACs Share a Common Mechanism of Regulation by Inositol Phosphates

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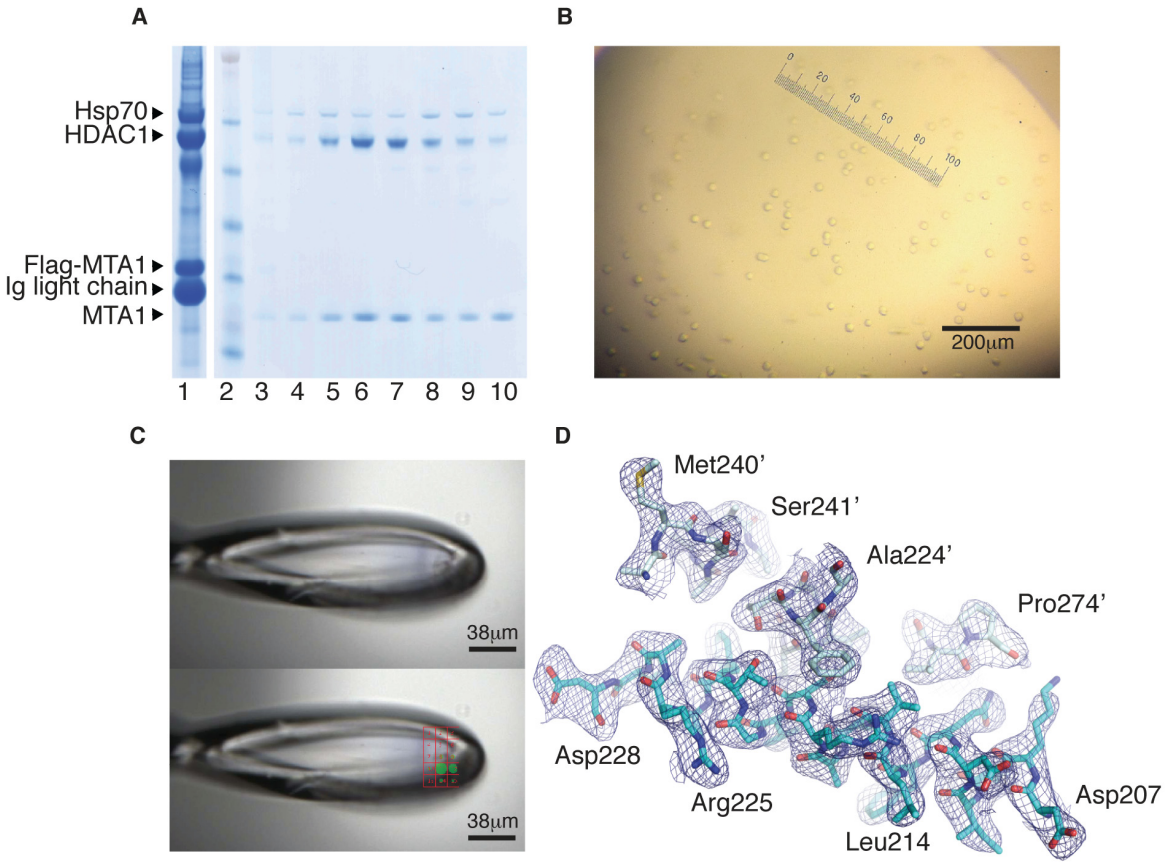

Figure S1. Expression, purification and crystallisation of the HDAC1:MTA1 complex, Related to Table 1 and Figure 1

(A) SDS-PAGE gel showing the purification of the HDAC1:MTA1 complex on FLAG resin followed by gel filtration. Lane 1, the complex before TEV cleavage; Lane 2, SeeBlue Plus2 pre-stained markers (Invitrogen); 14kDa, 17kDa (purple), 28kDa, 38kDa, 49kDa, 62kDa, 98kDa (orange); Lane 3-10, gel filtration fractions after TEV cleavage with peak elution of the complex in lane 6. **(B)** Crystals of the HDAC1:MTA1 complex. **(C)** Single crystal mounted at the DIAMOND synchrotron microfocus beamline (I24) showing use of the fast grid-scan tool to centre the crystal. Diffraction score is indicated by the diameter of the green circle. **(D)** Electron density (2Fo-Fc) contoured at 1σ showing the MTA1 dimer interface.

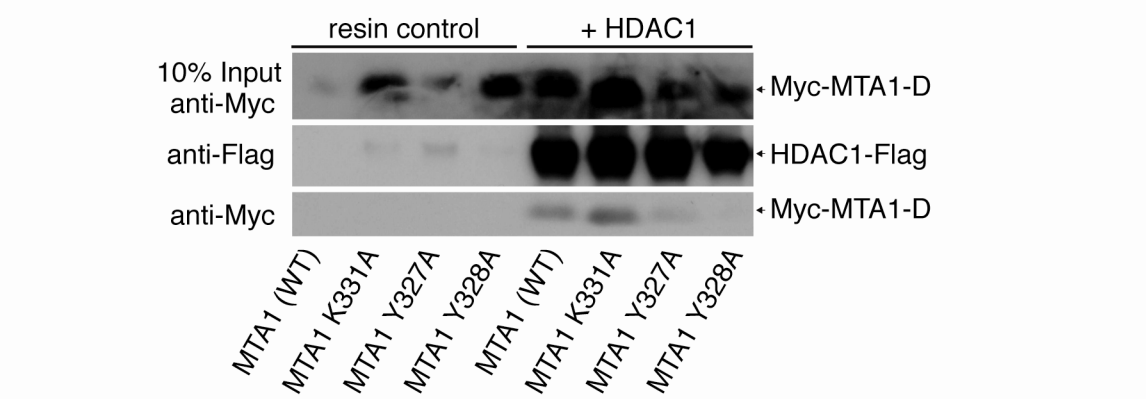

Figure S2. The HDAC1-FLAG:MYC-MTA-D (SANT domain) interaction can be perturbed by mutation of IP binding residues Y327A and Y328A, but not K331A, Related to Figure 2
Proteins were immunoprecipitated on FLAG resin and detected with anti-MYC and anti-FLAG.

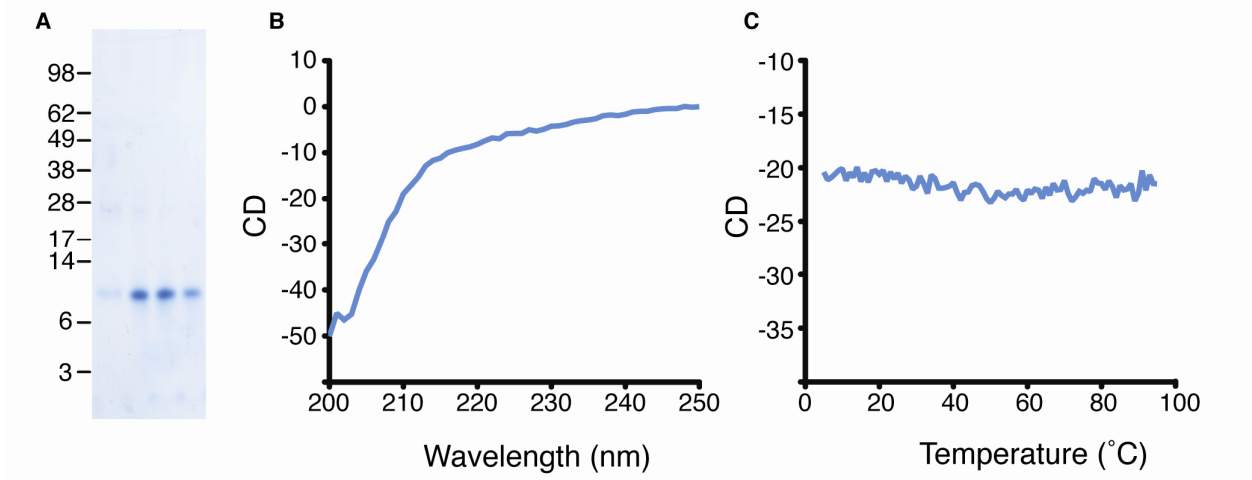

Figure S3. The ELM2-dimerisation domain of MTA1 shows little or no secondary structure in the absence of HDAC1, Related to Figure 1
(A) Comassie gel showing gel filtration fractions of E.coli-expressed ELM2-dimerisation domain of MTA1 (aa 205-310**). (B)** CD spectrum of MTA1 at 1mg/ml, in the absence of HDAC1. **(C)** CD denaturation curve of MTA1. Molar ellipicity was monitored at 210nm.

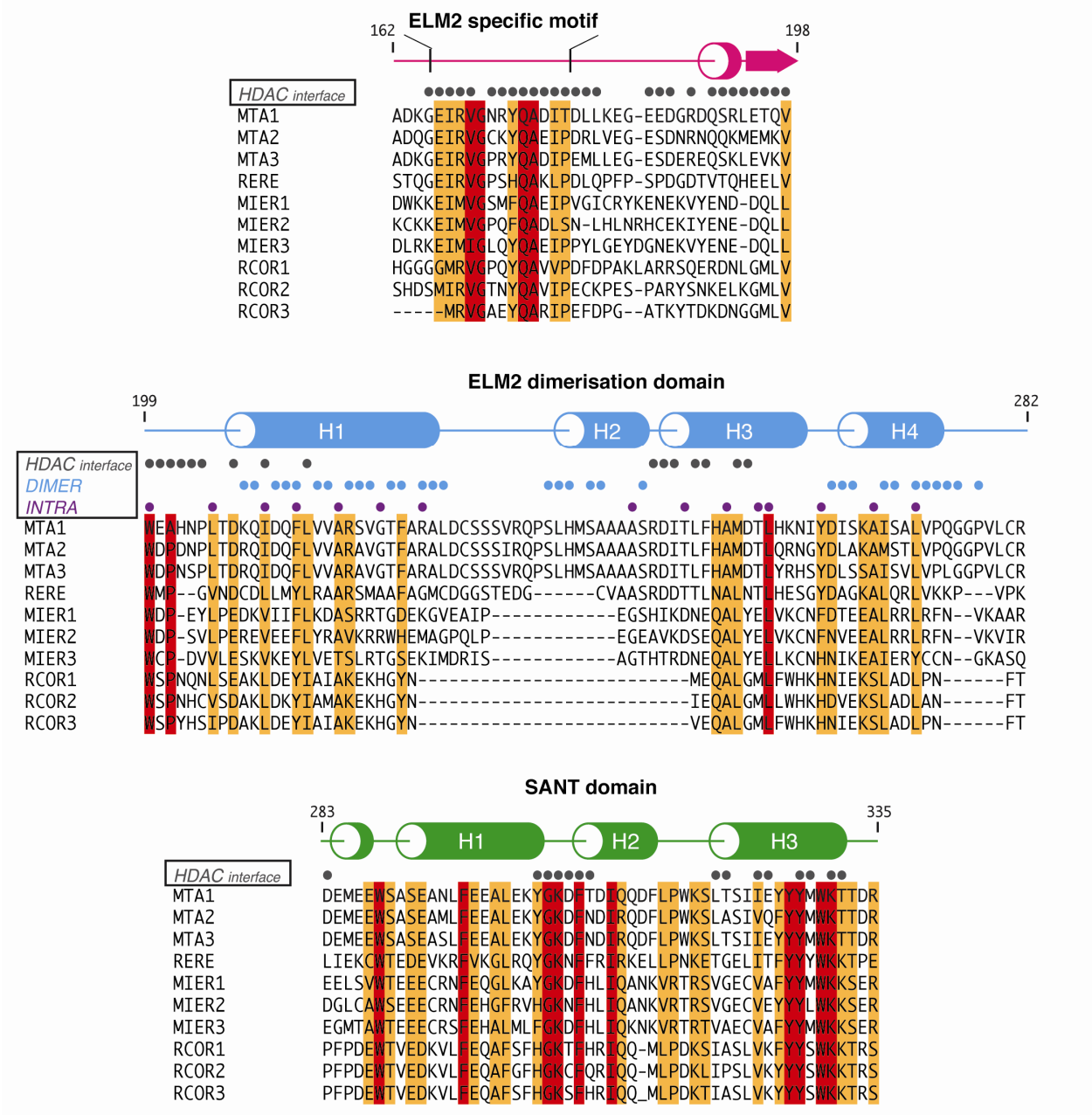

Figure S4. Sequence alignment of the ELM2 and SANT domains from 10 corepressor proteins, Related to Figures 1 and 2

Identical residues are highlighted in red and conserved residues are highlighted in orange. Grey dots above the sequence alignment show MTA1 residues involved in binding to HDAC1, cyan dots show MTA1 residues found at the dimer interface, and purple dots show MTA1 residues involved in forming the ELM2 helical bundle. The secondary structure of MTA1 is indicated above the sequences and the ELM2 specific motif is highlighted.

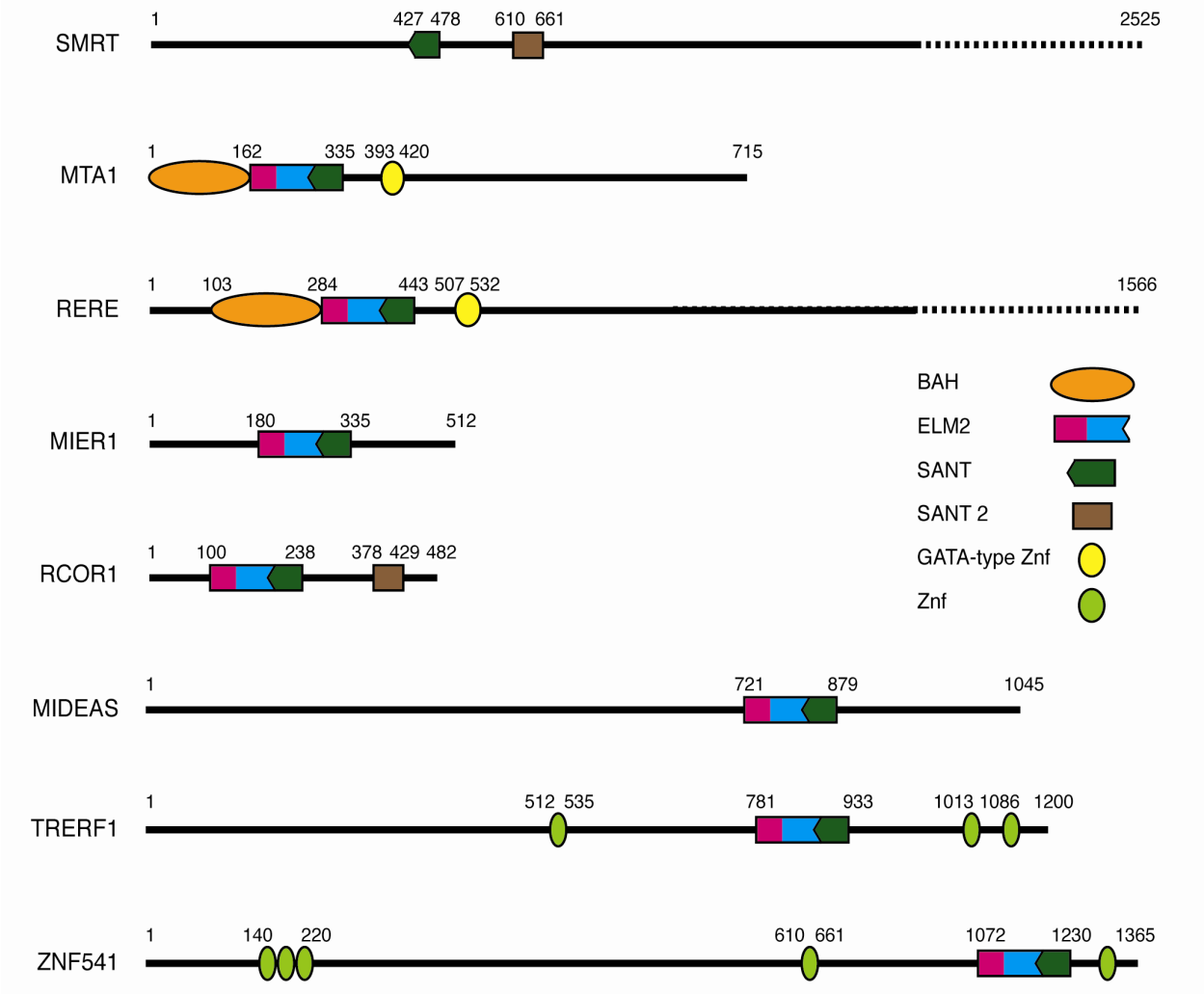

Figure S5. Schematic domain structures of SMRT, MTA1, RERE, MIER1, RCOR1 MIDEAS, TRERF1 and ZNF541, Related to Figure 7