



Supplementary information, Figure S3 D14 adopts almost identical surface conformations in its four different states. Structure overlays of apo D14 (PDB 4IH4, grey) with either GR24-bound D14 (blue), D14 covalently bound to the GR24 hydrolysis intermediate (PDB 4IHA, magenta), or D14 bound to the D-ring GR24 hydrolysis product (PDB 3WIO, pink). **(A)** Ribbon presentations, **(B)** Transparent ribbon presentations with the lid domain highlighted in yellow and surface residues identified mutationally as critical for D3 interaction shown in stick presentation overlaid on the residues of D14 shown in green. Note that the different conformation of E140 in the structure of hydrolysis product-bound D14 is due to crystal packing as E140 of apo D14 from the same crystal adopted the identical conformation (see Suppl. Fig. 2). Ligands in (A) are shown as Van der Waals spheres.