Supplementary Data

Acetylation of Lysine 109 Modulates Pregnane X Receptor DNA Binding and Transcriptional Activity

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Figure 1: Pairwise sequence alignment of PPAR-γ with human PXR is shown with the position of K155 (of PPAR-γ) and K109 (PXR) that are predicted to be acetylated indicated with arrows.

Figure 2: Structural superpositioning of PXR LBD (in orange ribbons) derived from the crystal structure complex of PXR-RXR (pdb code: 4j5w) with the full length modeled PXR structure (in pink ribbons) is shown. Note, the LBD of the model superimposes with a rmsd of 0.8 Ã̃.

Figure 3: Structural superpositioning of the wild type PXR (light pink)-DNA(green-red)-RXR (orange) on to the model of K109-Ac PXR (red)-DNA (gren-red)-RXR (orange) is shown in cartoon format with K109 in both models represented as ball and sticks and colored atom type (C-grey, N-blue,O-red, H-white). The co-factors and antagonist peptide are shown as magenta and cyan ribbons.

Coordinates of PXR-RXR-DNA model in PDB format is provided as an attachment. Please note, since the coordinates for PXR are numbered from residue 1 instead of 37, K109 will be K72.

Figure 1

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PPAR-g          MGETLGDSPIDPESDSFTDTLSANISQEMTMVDTEMPFWPTNFGISSVDLSVMEDHSHSF 60
PXR             -----------------------------------------------------------M 1
                                                                           :

PPAR-g          DIKPFTTVDFSSISTPHYEDIPFTRTDPVVADYKYDLKLQEYQSAIKVEPASPPYYSEKT 120
PXR             EVRPKE--SWNHADFVHCEDTESVPGKPSVN----------------------------- 30
                :::*    .:.  .  * **   .  .* *

PPAR-g          QLYNKPHEEPSNSLMAIECRVCGDKASGFHYGVHACEGCKGFFRRTIR--LKLIYDRCDL 178
PXR             -----ADEEVGG---PQICRVCGDKATGYHFNVMTCEGCKGFFRRAMKRNARLRCPFRKG 82
                     . ** ..   .  ********:*:*:.* :**********:::   :*     .

PPAR-g          NCRIHKKSRNKCQYCRFQKCLAVGMSHNAIRFGRMPQAEKEKLLAEIS--SDIDQLNPE- 235
PXR             ACEITRKTRRQCQACRLRKCLESGMKKEMIMSDEAVEERRALIKRKKSERTGTQPLGVQG 142
                 *.* :*:*.:** **::***  **.   * . .  : .:  :  : *  :. : *. :

PPAR-g          -SADLRALAKHLYDSYIKSFPLTKAKAR-----AILTG------------------KTTD 271
PXR             LTEEQRMMIRELMDAQMKTFDTTFSHFKNFRLPGVLSSGCELPESLQAPSREEAAKWSQV 202
                 : : * : :.* *: :*:*  * :: :     .:*:.                   :

PPAR-g          KSPFVIYDMNSLMMGEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSI 331
PXR             RKDLCSLKVSLQLRGEDGSVWNYKPPADSGGKEIFS-LLPHMADMSTYMFKGIISFAKVI 261
                :. :   .:.  : ***   ::: .* :. .**:   ::      *.  .: * .:** *

PPAR-g          PGFVNLDLNDQVTLLKYGVHEIIYTMLASLMNKDGVLISEGQGFMTREFLKSLRKPFGDF 391
PXR             SYFRDLPIEDQISLLKGAAFELCQLRFNTVFNAETGTWECGR--LSYCLEDTAGGFQQLL 319
                . * :* ::**::*** ...*:    : :::* :    . *:  ::  : .:       :

PPAR-g          MEPKFEFAVKFNALELDDSDLAIFIAVIILSGDRPGLLNVKPIEDIQDNLLQALELQLKL 451
PXR             LEPMLKFHYMLKKLQLHEEEYVLMQAISLFSPDRPGVLQHRVVDQLQEQFAITLKSYIEC 379
                :** ::*   :: *:*.:.: .:: *: ::* ****:*: : ::::*:::  :*:  ::

PPAR-g          NHPESSQ--LFAKLLQKMTDLRQIVTEHVQLLQVIKKTETDMSLHPLLQEIYKDLY- 505
PXR             NRPQPAHRFLFLKIMAMLTELRSINAQHTQRLLRIQDIHP--FATPLMQELFGITGS 434
                *:*:.::  ** *::  :*:**.* ::*.* *  *:. ..     **:**::
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Figure 2

Figure 3