L.A.25

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Structure analysis of ligand-independent activation of Fushi tarazu factor-1 ligand binding domain from *Drosophila melaganoster.*

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Drosophila melanogaster Fushi tarazu factor 1 (FTZ-F1) is an orphan nuclear receptor of which ligand has not been identified until now. The FTZ-F1 regulate gene expression for development, reproduction and cholesterol homeostasis. Also, It is known that the FTZ-F1 interacts with segmentation gene '*Fushi tarazu*' (*FTZ*) for activation of the FTZ-F1. The FTZ-F1 is divided two parts, DNA-binding domain (DBD) and ligand-binding domain (LBD). It is known which ligand binding domain of FTZ-F1 is crucial part to regulate gene expression. Here we report the crystal structure analysis of the FTZ-F1 LBD bound to the peptide containing LXXLL co-activator motif of FTZ. The FTZ-F1 LBD structure consists of twelve α-helices and two β- strands which form a fourth-layer alpha-helical sandwich. Compared with structures of Liver receptor holmologue-1 and Steroidogenic factor-1 in the same subfamily of nuclear receptor, the FTZ-F1 LBD does not have an enough space for ligand-binding which explains in structural points why the ligand for FTZ-F1 regulation have not been found even though extensive efforts searching for it. Interestingly FTZ-F1 has the AF-2 in the active conformation without ligand binding. With mutagenesis assays, these suggest that Ftz-F1 is a constitutively active nuclear receptor which does not need ligand implying the another regulation mechanism of the FTZ-F1.

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Keywords: FTZ-F1, orphan nuclear receptor, DNA-binding domain (DBD)

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Crystal structure of human TERT_ NLS peptide in complex with hImportin α5.

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hTERT is a catalytic component of telomerase that can extend the telomere end of genomic DNA. This protein has been shown to highly express in tumor cell. Residue S227 of hTERT is phosphorylated by Akt kinase [1] and hTERT is strongly localized to the nucleus. hTERT has a nuclear localization signal (NLS) from G220 to A242 containing two basic regions which might interact with hImportin α with bipartite binding mode. We used isothermal titration calorimetry (ITC) to determine the specificity of hImportin α5 comfirming the effect of phosphorylation on binding affinity. As a result, Phosphorylated hTERT S227 is higher affinity than un-phosphorylated hTERT. To see the molecular mechanism in detail, the complex structure of hTERT_NLS peptide and hImportin α5 has been solved at a resolution at 2.4Å. As might be expected, hTERT_NLS is shown to interact with hImportin α5 with bipartite binding mode. Phosphorylated S227 of hTERT interacts with R395 of hImportin α5 by hydrogen bond, which explains increased affinity by phosphorylation resulting in more efficient nuclear localization of telomerase. This result suggests that phosphorylation of TERT is a regulation strategy of localization for telomerase activity control.

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Keywords: human TERT, human Importin, NLS (nuclear localization signal), ITC (Isothermal titration calorimetry)

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Controlled Crystallization of organic molecules on Micro-patterned Surfaces.

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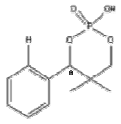
The possibility to control the crystallization process using self-assembled monolayers is an extremely interesting and promising approach in organic materials [1]. This control has achieved by the use of inorganic crystalline substrates where nucleation is induced via epitaxy, although organic single crystals and Self assembled monolayers (SAMs) have been used to control the polymorphic selectivity of the compound to crystallize, which is based in the lattice match between the molecular cluster and crystalline substrate terraces [2]. According to this concept, Self assembled monolayers (SAMs) have been used as controlled nucleation centers [3].

Here, we show the controlled crystallization of the compound Phencyphos on different functionalized surfaces, and show the differences between homogenous SAMs and mixed SAMs (Microcontact printing method). On micropatterned surfaces (mixed SAMs), Phencyphos crystallizes following a preferential orientation while on functionalized surfaces (homogeneous SAMs), Phencyphos crystallizes following different orientations (Figure).



Phencyphos.

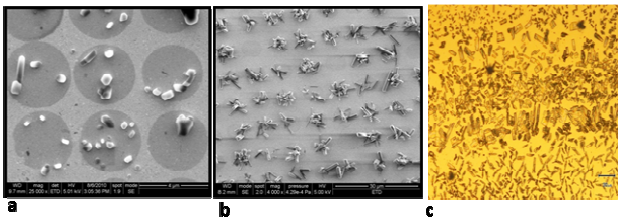


Figure. (a) (+)Phencyphos grown on micropatterned surface (SEM image). (b) (-) Phencyphos grown on micropatterned surface (SEM image). (c) (+)Phencyphos grown on homogeneous SAMs on surface (Optical Microscope image).

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Keywords: Surfaces, Interfaces, Growth.