

Identification and characterisation of the importin complexes involved in the nuclear translocation of the aryl hydrocarbon receptor

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Abstract

The aryl hydrocarbon receptor (AHR) is a ligand-dependent transcription factor that mediates a broad spectrum of physiological processes in response to numerous substances including chemical pollutants, natural products and endogenous metabolites. Upon ligand binding, AHR undergoes translocation to the nucleus where it can regulate expression of different genes. The transport into the nucleus relies on the specific interactions with the complexes of the importin proteins. So far, we are lacking the detailed description of the mechanisms governing these interactions.

In order to address this issue, we expressed and purified all seven members of the human importin alpha family as well as the importin beta. Using immunoprecipitation technique, we identified the importin complexes involved in the interactions with AHR. We validated our findings using analytical size exclusion chromatography. We also analysed the interactions using fluorescence anisotropy. Structural characterisation of the complexes using X-ray crystallography and cryo-EM is currently under way. Our data provide the first insights into the mechanisms governing the nuclear translocation of AHR.