S33-2 The subcellular localization mechanism of nuclear receptor CAR

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Animals including human beings have a defense mechanism against the toxicity of xenobiotics such as medicinal compounds and environmental pollutants. The receptor-type transcriptional factors, such as aryl hydrocarbon receptor (AhR), constitutive androstane receptor (CAR) and pregnane X receptor (PXR), play an important role in the defense against the toxicities of xenobiotics. These receptors are distributed predominantly in the cytoplasmic compartment without any stimuli. Following xenobiotic stimuli, receptors translocate into the nucleus and transactivate its target genes. However, the exogenously expressed CAR translocates spontaneously into the nucleus in immortal cells. Previously, we identified subcellular localization signals in rat CAR: nuclear localization signal (NLS), nuclear export signal(NES) and cytoplasmic retention region (CRR). Lack of the function of CRR might be responsible for the spontaneous nuclear accumulation of CAR in immortal cells. Knowing the mechanisms of the nuclear translocation of CAR would be useful for the establishment of novel assay systems for the screening of ligands and activators of CAR using immortal cells without sacrificing animals.