

## Role of the 4-5S binding protein in the induction of aryl hydrocarbon hydroxylase in the rat

M.Harris, C.Kamps and S.Safe<sup>1</sup>

Departments of Veterinary Physiology and Pharmacology, and Biochemistry and Biophysics, Texas A&M University, College Station, TX 77843, USA

<sup>1</sup>To whom reprint requests should be sent

**Analysis of male Sprague–Dawley rat hepatic cytosol from two commercial animal laboratories for the polycyclic aromatic hydrocarbon (PAH) 4-5S binding protein showed that in one group of animals no 4-5S protein was detectable (–4S) whereas the levels of this protein were  $208 \pm 57$  fmol/mg cytosolic protein in the +4S rats. The role of the 4-5S binding protein in the transregulation of the cytochrome P-450-dependent monooxygenase, aryl hydrocarbon hydroxylase (AHH), was therefore investigated in the –4S and +4S Sprague–Dawley rats. The dose–response curves for the induction of hepatic microsomal AHH by 3-methylcholanthrene (MC) were indistinguishable in both +4S and –4S rats and comparable results were observed for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) as an inducer. Both MC and TCDD exhibit high binding affinities for the aryl hydrocarbon (Ah) 8-9S receptor protein, whereas MC but not TCDD bound with high affinity to the 4-5S binding protein. Benzo[*a*]pyrene (B[*a*]P) binds with moderate affinity to both the Ah receptor and 4-5S binding protein and induces AHH in both –4S and +4S rats. Perylene binds with moderate affinity to the 4-5S binding protein but does not interact with the Ah receptor. This PAH was inactive as an inducer of AHH in +4S and –4S Sprague–Dawley rats. These results show that there was a correlation between the Ah receptor binding affinities of MC, B[*a*]P and perylene and their potencies as AHH inducers in Sprague–Dawley rats, and this corresponds to previous correlations for the induction of AHH in rat hepatoma H-4-II E cells in culture. In contrast no such correlations existed between the AHH induction potencies of these polynuclear aromatic hydrocarbons and their affinities for the 4-5S binding protein. These data, coupled with the fact that the absence of the 4-5S binding protein in the –4S Sprague–Dawley rats did not affect AHH inducibility by MC, B[*a*]P or perylene, suggests that the 4-5S binding protein does not play a role in the transregulation of cytochrome P-4501A1 in the rat or rat hepatoma cells in culture.**