## EPHAR 2001 – LYON 6<sup>th</sup> – 9<sup>th</sup> July

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Binding of pharmacological results to cloned abstract forms

V. Rapamil, <u>A. Denosine</u>, and P. Nicilline. National Institute of Pharmacology, 75000 Paris, France.

Specific binding of pharmacological results to on-line abstract forms has not been widely studied. Thus, pharmacological results were radiolabelled <sup>12</sup>Times and incubated in the present of 10<sup>1</sup> cloned EPHAR forms expressed in recombinant FCP cells. Results demonstrate that specific binding markedly increased by strict respect of the instruction for submission of the.....

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The tyrosine kinase inhibitor Tyrphostin AG126 reduces the renal dysfunction associated with ischaemia/reperfusion of rat kidneys *in vivo* 

P.K. Chatterjee, N. Patel, E. Kvale, C. Thiemermann. Dept. Exp. Med. & Nephrol., The William Harvey Research Institute, London, EC1M 6BQ, U.K. Tyrosine kinases play an important role in the regulation of several genes including inducible nitric oxide synthase (iNOS) which contributes to renal ischaemia/reperfusion (I/R) injury via the production of nitric oxide (NO). We investigated whether the tyrosine kinase inhibitor Tyrphostin (Tyr) AG126 could reduce the renal dysfunction mediated by I/R of rat kidneys. Renal pedicles of male Wistar rats were clamped for 45 min followed by reperfusion for 6 h in the absence (Control) or presence (Tyr AG126) of Tyr AG126 (5 mg/kg i.p. bolus administered 30 min prior to I/R). Sham animals did not undergo bilateral renal clamping (Sham). Plasma levels of urea (P<sub>Ur</sub>) and creatinine (P<sub>Cr</sub>) were used as indicators or glomerular dysfunction. Creatinine clearance (C<sub>CL</sub>) and fractional excretion of Na<sup>+</sup> (FE<sub>Na</sub>), estimated using plasma and urinary parameters, were used as indicators of glomerular and tubular function, respectively. Data below expressed as mean  $\pm$  SEM, analysed using one-way ANOVA followed by Bonferroni's testing. \*P<0.05 vs Control.

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Group	N	$P_{Ur}$	$P_{Cr}$	$\mathbf{C}_{\mathbf{CL}}$	$FE_{Na}$
		(mmol/L)	(µmol/L)	(ml/min)	(%)
Sham	8	5 ± 1*	41 ± 4 <b>*</b>	$1.43 \pm 0.27$ *	1.1 ± 0.3*
Control	7	$24 \pm 1$	$199 \pm 6$	$0.01 \pm 0.004$	$58 \pm 12$
Tyr AG126	11	18 ± 2*	159 ± 8*	$0.05 \pm 0.01$ *	19 ± 3*

These data suggest that Tyrphostin AG126 significantly reduces the renal dysfunction associated with I/R of rat kidneys. This beneficial action is likely to be mediated via inhibition of tyrosine kinase activity and subsequent reduction of iNOS expression and NO production.