

ANG II and JAK2 interactions in hypertension

A major focus of my lab is ANG II and JAK2 interactions in hypertension. We have chronically catheterized rats and measured mean arterial pressure 24 hrs/day. In these animals we administered ANG II (10 ng/kg/min) and the JAK2 inhibitor AG490 (10 ng/kg/min). We found that treatment with AG490 prevented the development of hypertension. The mechanisms for this are not yet clear but this is the first study to clearly implicate JAK2 as a critical molecular component of ANG II's ability to cause hypertension. Future studies include determining the role of JAK2 in kidney function looking at vascular vs tubular effects. Additionally, determining the mechanisms by which JAK2 is involved in the increase in pressure and whether inhibiting JAK2 in an established model of hypertension can lower blood pressure and protect against further development of end-organ damage are also future areas of research I am pursuing in my K99/R00 grant application. Determining whether the elevation of JAK2 occurs in all models of hypertension or whether this is specific to ANG II and what the molecular mechanisms involved for activation and regulation of the JAK/STAT pathway in these disease conditions are is an area of research we are pursuing.