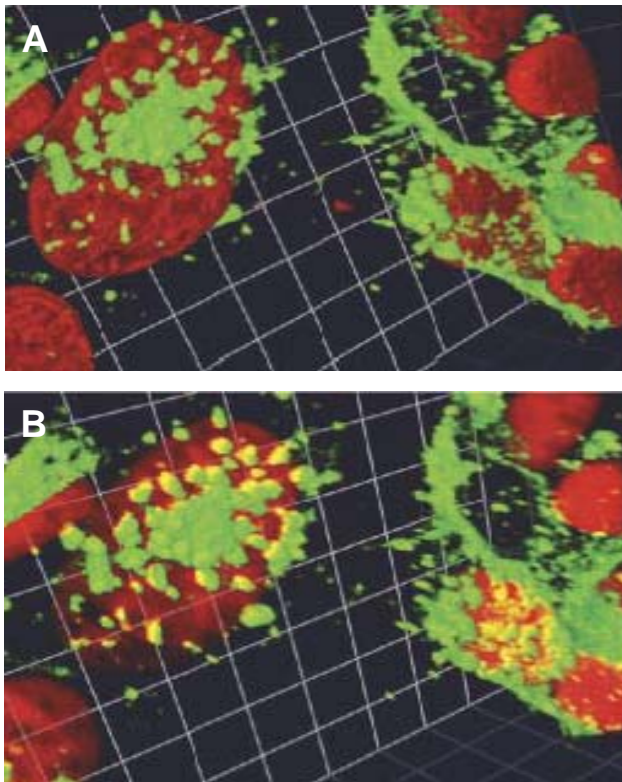




3D imaging of nuclear trafficking of the angiotensin II type 1A receptor



The Figure shows a 3D reconstruction rendered in **Volocity Visualization** of $AT_{1A}R$ /GFP trafficking. Receptors are displayed in green, nuclei are indicated by staining with DRAQ5 (red) and are shown at a density of 100% (A) or 50% (B). Interaction between the receptor and the nuclei is indicated in yellow. Calibration grid is 5 μ m/U

Dr Thomas Morinelli and colleagues are interested in the etiology of renal-vascular disease processes. They are studying the role of various endogenous vasoactive hormones with a special focus on angiotensin II (ANG II) and its G protein-coupled receptor (ANG II $AT_{1A}R$). ANG II, the effector molecule of the renin-angiotensin system (RAS), exerts hemodynamic and renal actions but also has profound effects on endothelial and smooth muscle cells. It is involved in blood pressure and fluid electrolyte regulation and disorders of the RAS contribute importantly to the pathophysiology of hypertension, congestive heart failure and renal disease.

Utilizing a GFP construct of the wild-type receptor $AT_{1A}R$ and DRAQ5 nuclear staining, receptor expression was characterized using laser scanning confocal microscopy. Z stacks of images were acquired through the sample and 3D rendered in **Volocity Visualization**. The researchers were able to demonstrate receptor internalization and localization to the nucleus, subsequent to ANG II stimulation. The figure shows a three dimensional visualization of $AT_{1A}R$ /GFP trafficking. **Volocity Visualization** allowed the researchers to vary the voxel opacity (volume pixels) in the 3D rendering. When the opacity is set to 100%, the voxels from the red nuclear channel appear as solid nuclei (red) with green receptors at the surface. When the opacity level of the red channel was reduced to 50%, surface localization was seen as being integrated into the nuclear area, as indicated by the yellow color.

Along with other well known membrane bound receptors, nuclear receptors for ANG II were described two decades ago. **Volocity Visualization** enabled Morinelli and co-workers to demonstrate nuclear trafficking of the stimulated $AT_{1A}R$. Further studies showed that nuclear localization of the activated receptor plays a key role in the initiation and amplification of pathobiological events that lead to vascular disease.

Since a blockade of the RAS through its receptors often constitutes the first line of treatment for hypertension and renal injury, further investigations of the presence of nuclear receptors and its functionality will improve the understanding and development of present therapies.