

## **STRUCTURAL MAPPING OF THE INSULIN RECEPTOR BY IN SITU SCANNING PROBE MICROSCOPY**

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A 450 kDa disulphide linked heterodimer single-pass transmembrane protein, the insulin receptor is autophosphorylated upon insulin binding to its extracellular domain. Remarkably, the structural basis for this activation process remained largely unknown until the recent electron cryomicroscopy studies of the insulin-insulin receptor complex by Luo et al. (Science, 1999, 285, 1077). We report here the results of an in situ study by high resolution scanning probe microscopy of the full-length insulin receptor reconstituted within supported planar lipid bilayers. Our preliminary studies confirmed that (1) the intact receptor could be reconstituted constitutively within a lipid vesicle; (2) fusion of the receptor-containing vesicles to mica resulted in the formation of molecular flat 5.5 nm thick supported planar bilayers populated by two populations of protrusions, the shape and size of which are consistent with those of the insulin receptor's intra- and extra-cellular domains as modelled by the STEM data of Luo et al. The results establish the framework for real-time studies of insulin binding to the receptor and direct mapping of insulin-insulin receptor binding forces by single molecule force spectroscopy.