Development of optogenetic insulin receptor system in living mice liver

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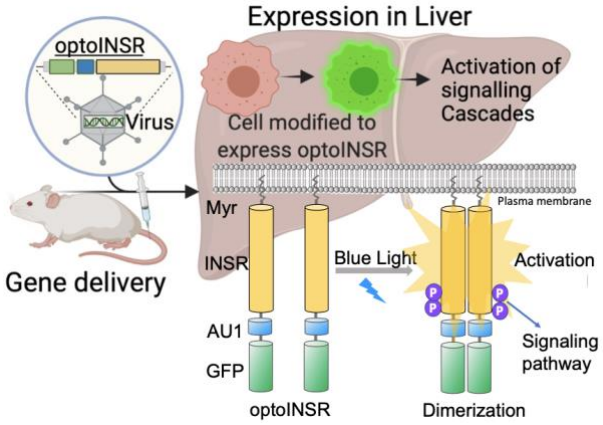
Insulin and insulin receptor (INSR) play a key role in the hormonal regulation system to maintain glucose homeostasis.[1] Secreted by the pancreatic islet beta cells, insulin is released into the bloodstream in several different temporal patterns.[2] To date, the detailed functional role regards to insulin secretion patterns are yet to be confirmed due to the constraint of the conventional methods. In this work, we report an opto-insulin receptor (optoINSR) system that enables the optical activation of insulin signaling using blue light illumination in vivo.

Activation of the insulin signaling cascade begins with the binding of insulin to the α subunits of INSR. Subsequently, the structural rearrangement brings the β subunit close together to activate downstream signaling cascades. Simulating this process, optoINSR consists of the β subunit of the INSR that is connected to the photoreceptorAureochrome1a (AU1) from Vaucheria frigida.[3] Using blue light, AU1 dimerizes due to light-induced conformational changes in the chromophore, bringing the fused βsubunits together. OptoINSR enables the activation of the insulin signaling cascade in the targeted illumination area. Nevertheless, adenovirus (AdV) vectors containing optoINSR gene were injected in vivo into living mice to induce liver expression. The infected mice were then exposed for illumination through an abdominal incision. From the western blotting result obtained from the harvested liver in the illuminated area, we have confirmed the phosphorylation of downstream molecules upon light irradiation. The liver section image confirmed the functional expression of optoINSR in hepatocytes in all areas of the liver. With this system, we achieved artificial manipulation of insulin signaling in living mice with external light.



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