



Signal decoding in GPCR networks: from method development to pathway-selective manipulation

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Our research illuminates the molecular mechanisms underlying GPCR signaling diversity and its regulation. We have developed methodologies for high-throughput, user-friendly platforms for GPCR signaling, including a TGF α shedding assay and NanoBiT signal sensors. By combining these assays with a panel of GPCR-effector-knockout HEK293 cell lines, we can isolate complex signal crosstalk, enabling unprecedented analytical precision. In this seminar, I will present our suite of GPCR signal analysis methods and their application to understanding GPCR–G-protein-coupling selectivity. I will demonstrate the development of a G₁₂-selective DREADD, which provides valuable insights into G₁₂ signaling pharmacology *in vivo*. Additionally, I will highlight our recent investigations into membrane nanodomains and their critical roles in GPCR signaling regulation, as revealed through single-molecule observations in living cells. These findings have significant implications for fundamental medical research and open promising new avenues for drug discovery.

Host: Yasunori Hayashi x84393