

## 糖リン酸の単一蛍光タンパク質ベースバイオセンサーの開発へ

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### Towards the development of single fluorescent protein-based biosensors for sugar phosphates

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Sugar phosphates (SPs) are the cornerstone of metabolic pathways such as glycolysis and the pentose phosphate pathway (PPP)<sup>1,2</sup>. For example, glucose-6-phosphate (G6P) is a precursor to other SPs, including glycerol-3-phosphate (G3P), which are used to produce metabolites (e.g. lactate), energy carriers (e.g. ATP), and lipids (e.g. phospholipids). Importantly, recent studies have reported that sugar metabolism is dysregulated in certain neurodegenerative diseases<sup>3</sup> and cancer development<sup>4</sup>. While biosensors for sugars and metabolites, namely glucose and lactate, have been constructed<sup>5</sup>, no biosensors targeting SPs exist. The development of SP biosensors would aid in interrogating sugar metabolism at a finer level.

Here, we focus on engineering single fluorescent protein (FP)-based biosensor prototypes for SPs by employing a transposon-mediated approach<sup>6</sup> for library construction. Briefly, a transposon is inserted into a gene encoding an SP binding protein at random sites and subsequently replaced with an FP. This process generates a library of biosensors which is narrowed down to select candidates using high-throughput screening methods. Currently, our work focuses on the development of a G6P biosensor and G3P biosensor based on G6P-binding protein afuA<sup>7</sup> and G3P-binding protein ugpB<sup>8</sup>, respectively. Ultimately, we envision the application of our biosensors in neurodegenerative disease research.

**Keywords :** *single fluorescent protein-based biosensor, transposon-mediated approach, sugar phosphate biosensor*

糖リン酸は解糖系などの代謝過程の根幹をなす分子である<sup>1,2</sup>。例を挙げるとグルコース 6 リン酸 (G6P) は他の糖リン酸の前駆体であり、乳酸等の代謝物や ATP 等のエネルギー担体の生成のために用いられる。先行研究で糖代謝が神経変性疾患<sup>3</sup>とがん発生<sup>4</sup>で異常に調節されることが示されているが、現在までに糖リン酸を標的としたバイオセンサーの報告はない<sup>5</sup>。そこで本研究では、糖リン酸の単一蛍光タンパク質ベースバイオセンサーの開発を目指した。具体的には、トランスポゾンを用いた方法<sup>6</sup>によって蛍光タンパク質をランダムに糖リン酸結合タンパク質<sup>7,8</sup>中に挿入したライブラリを作製し、ハイスループットな蛍光評価によって有望な分子を選抜中である。将来的には、神経変性疾患の研究への応用も視野に入れている。

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