Highly Selective Optical Biosensors for Proteins in Biological Samples, with Excellent Signal-to-Noise Ratio (Yeda)

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Summary

Sensing the levels of protein-based biomarkers in biological samples is crucial for diagnosis of various diseases including cancer. Optical biosensors offer sensitivity and cost-effectiveness; however, current commercially available devices fail to provide sufficient selectivity and signal to noise ratios for protein targets. The technology presents an approach for obtaining sensitive and widely applicable method for detecting and labeling a wide range of proteins in their native environment. It is based on the modification of thiazole orange with one or several protein binders. The result is a series of fluorescent molecular sensors customized to detect various proteins in bio-fluids and living cells with excellent signal-to-noise ratios.Selective even towards isoforms of the same protein, several such biosensors are now developed against key biomarkers of different cancers, such as Glutathione S-Transferases (GST), His-tag and more. Together, they represent a novel class of highly sensitive fluorescent protein sensors that can pave the way for accurate, high-throughput medical diagnostics and live cell imaging.

Applications

Detection of proteins in biological samples for medical diagnostics Fluorescent detection of His-tag or GST labeled proteins for imaging in living cells Differentiating between protein isoforms

Advantages

High S/N - signal to noise ratio High selectivity - enables to detect even different isoforms of the same target Compatible with biological samples and living cells

Technology's Essence

Asymmetrical cyanine dyes constitute a unique class of fluorescent molecular sensors whose activation does not involve FRET, ICT, or PET processes. Instead, their fluorescence emission is turned on upon restriction of their torsional motion. Upon binding to DNA or peptide aptamers, this torsional motion leads to an enhanced fluorescence signal.The present inention, developed by Dr. David Marguleis and his team, is based on TO derivatives linked to a specific "protein binder" - a molecule that selectively binds a desired target protein. The result is a highly selective series of sensors, able to detect their target biomarkers at nanomolar concentrations, with excellent S/N (signal-to-noise) ratios. With simple structural modifications, these sensors can be adjusted to distinct even between different isoforms of the same target, highlighting their strong selectivity.Most importantly, sensing is compatible with diverse types of biological media including serum, blood, urine, saliva and other body fluids samples, rendering them especially suitable for medical applications. Currently, the team is developing TO-sensors for **GST, MMPs, PSA**, **Estrogen receptor**, **Fibronectin** , **Fgf** and **PDGF** - known biomarkers of different cancers, **b-amyloid** - a known biomarker of Alzheimer's disease, **Caspases**, **HDAC** and **His-tag**. Such sensor for His-tag may be used as a powerfull research tool, to circumvent the limitations of common labeling methods, in living cells.

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