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RNA detection in living cancer cells by far-red emitting PNA-FIT probes

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To diagnose cancer early on has no doubt a huge impact on the success rate of anticancer therapy in almost all clinical settings. One promising approach is based on the detection of RNA biomarkers; particularly, mutated RNA that gives a distinct signature and allows a better choice of treatment. One attractive approach is based on the use of FIT-PNA (forced intercalation – peptide nucleic acid) probes. These PNA molecules hybridize to complementary RNA and gain fluorescence only after binding to their RNA target. We have previously shown that such FIT-PNAs with TO (thiazole orange) as a surrogate base, fluoresce in living pancreatic cancer cells (Panc-1) that express mutated kRAS mRNA (G to A single point mutation at codon 12) but not so in colon cancer cells (HT-29) that express wild-type kRAS mRNA. Herein we report on the design and synthesis of a new surrogate base (BisQ) with the unique feature of far-red emission. This surrogate base was introduced into PNAs that target the mutated kRAS oncogene. PNAs with a short cell penetrating peptide (CPP) consisting of 4 D-Lysines were shown to readily penetrate living cancer cells and fluoresce in the far-red region (λ max = 609 nm) exclusively in pancreatic cancer cells (Panc-1) that express the mutated form of kRAS but not in pancreatic cancer cells that are non-mutated (wild type) in kRAS (BxPC-3). We are currently developing new FIT-PNA probes targeting other RNA biomarkers and exploring new surrogate bases with unique spectral properties.

Biography

Eylon Yavin has completed his PhD at the Weizmann Institute of Science (Israel). He did his Post-doctoral work at the laboratory of Prof. Jacqueline Barton at Caltech (CA, USA). In 2006, he joined the School of Pharmacy at Jerusalem as a faculty member. He is currently a Senoir Lecturer and has an active research lab in the field of Nucleic Acids. He has published more than 40 papers in reputed journals and has been recently elected as the President of The Medicinal Chemistry Section of the Israel Chemical Society.

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