Encoded Nanospheres as Biomarkers for the Early Detection of Cystic Fibrosis

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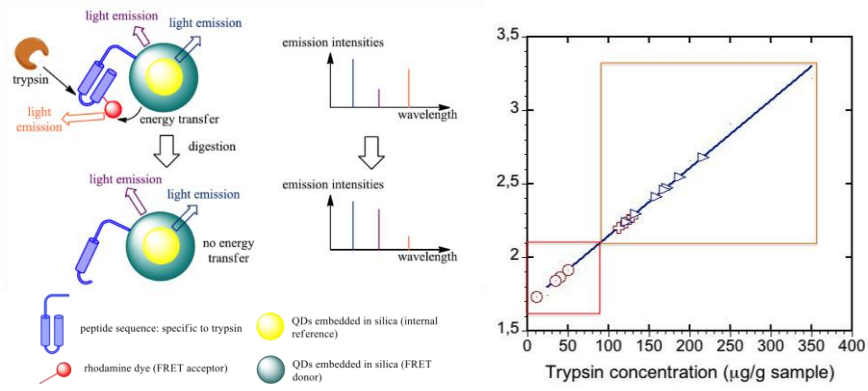
Cystic fibrosis (CF) is an autosomal recessive genetic disorder characterized by abnormal transport of chloride and sodium across an epithelium, leading to thick secretions, affecting lung, pancreas, liver and intestine. Current methods for the diagnosis of CF require long time analysis and further experimentation to provide accuracy. Such methods do not allow the determining the genotype of the patient.

We have developed a new sensitive biomarker in such a way that the optical response of the system upon light irradiation, when treated with faeces samples, can be directly correlated to trypsin concentration in the sample, an indicator of the genotype of the patient.[1] Our biomarker consists of two silica nanospheres arranged concentrically, one embedding a core of CdSe nanocrystals (CdSe660) with luminescence emission maximum at λ=660 nm, and the other one embedding the second type of CdSe nanocrystal with luminescence emission maximum at λ=540 nm (CdSe540). The outer silica surface is conjugated to a trypsin-specifically sensitive peptide which is labelled with a dye capable of absorbing the light emitted at 540 nm and emits a fluorescence signal via a FRET (Förster Resonance Energy Transfer) process. Upon excitation at λ=405 nm, both types of CdSe quantum dots undergo fluorescence emission and the FRET process takes place. In the presence of trypsin, the proteolytic enzyme activity leads to the peptide cleavage and the FRET process is disrupted. Thus, by measuring the signal increase at λ=540 nm, that corresponds to the CdSe540 emission once the peptide is cleaved, it is possible to correlate the changes in the emission intensity with the enzyme activity and amount using the constant emission intensity of CdSe660 as internal reference. Using our nanospheres in real samples, four participants to the study were confirmed homozygotic, while the other seven were heterozygotic for cystic fibrosis.



[1]. E. Palomares, G. Stoica, I. Castelló Serrano. *Ratiometric assay for hydrolytic enzyme quantification* (2013), EP13382239.