Fluorescent micro-RNA for cancer diagnostics

Biomarkers are indicators of biological states or conditions and can therefore provide important information about diseases such as cancer. In clinical diagnostics biomarkers are most often proteins or nucleic acids such as DNA or RNA. Biomarkers that can be found in the circulating blood (circulating biomarkers) are relatively easily accessible by a simple blood draw. However, they can often be found in only tiny amounts (concentrations) and several different biomarkers must be quantified for a correct and precise diagnosis. Relatively new circulating biomarkers are micro-RNAs, which are very important for disease development because they can alter the process of protein production in cells and thereby the biological functions of our body.

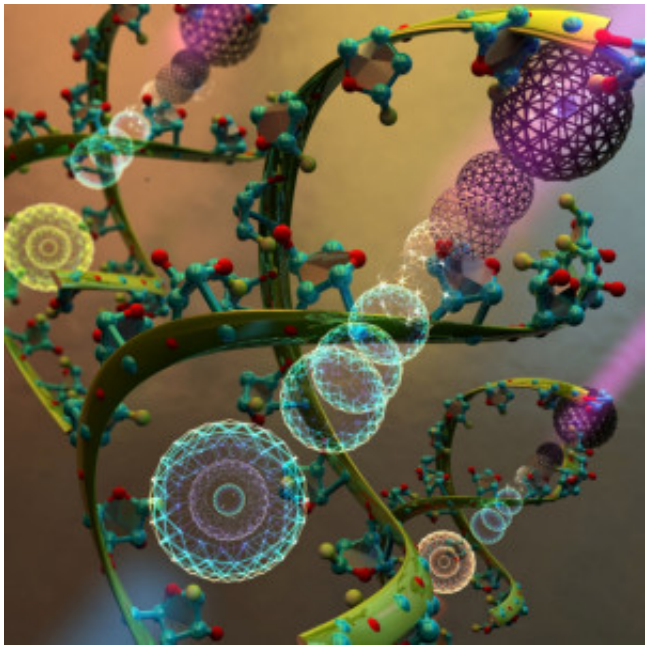

Fig. 1: Artistic illustration of three-color energy transfer in micro-RNA double helices

In a recent research study highlighted on the cover of the scientific journal Angewandte Chemie International Edition (Angew. Chem. Int. Ed. 2015, 54, 10024–10029) we describe the development of a rapid and simple optical test that can identify and quantify several different micro-RNAs from a single small volume liquid sample, which may be a human blood sample. The detection technology uses fluorescence or more precisely FRET, which stands for ”Förster Resonance Energy Transfer“ named after the scientist Theodor Förster. In FRET one fluorescent molecule can transfer its energy to another nearby fluorescent molecule and this results in the switching off of the first molecule’s fluorescence and the switching on of the second molecule’s fluorescence. As these two molecules usually have different fluorescence colors, the detection of color switching (e.g., violet fluorescence off and blue fluorescence on) can be used to indicate FRET.

How can this FRET be used to detect micro-RNA? Unlike DNA, which is usually found in a double-helix formed of two nucleic acid strands, RNA exists most often in a single strand. But also RNA can form double strands, and therefore one can hybridize (or bind) different single RNA strands to one another. In our detection technology the RNA strand of interest is the micro-RNA, which can be hybridized by two smaller RNAs (e.g., each having half the length of the micro-RNA). The hybridization of both smaller RNA strands to the micro-RNA is exclusive for only this micro-RNA. So if these two smaller RNAs carry the two FRET fluorescent molecules the color switch can be used to identify and quantify (by the color intensity) only this specific micro-RNA. And if one uses three different FRET fluorescent molecule pairs on the non-binding ends of three different small RNA strand pairs, then the simultaneous detection of three different micro-RNAs becomes possible, as schematically presented in Figure 2 (and in a more artistic illustration in Figure 1).

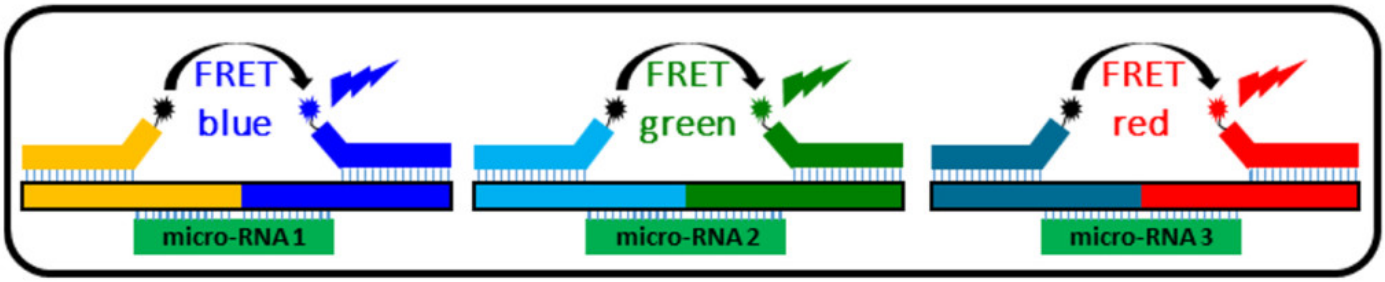

Fig. 2: Three-color FRET for the detection of three different micro-RNAs

In reality a large amount of biological engineering and biochemical, biophysical, and optical optimization combined with a sensitive detection technology was necessary to transform this scheme into a micro-RNA assay that can detect very tiny amounts of different (but still very similar) micro-RNAs from a single real-life blood sample. Our rapid, sensitive, and specific multiple micro-RNA fluorescence test may become a powerful tool for cancer diagnostics because it is much easier to use than the complicated detection formats that exist today. The addition of this new fluorescence assay to the toolbox of diagnostic tests will hopefully improve the versatility of clinical diagnostics and therefore the diagnosis and treatment of the many different types of cancers and other diseases

Niko Hildebrandt

NanoBioPhotonics, Université Paris-Sud, Orsay, France

Publication

A Rapid, Amplification-Free, and Sensitive Diagnostic Assay for Single-Step Multiplexed Fluorescence Detection of MicroRNA.
Jin Z, Geißler D, Qiu X1, Wegner KD, Hildebrandt N
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