The bridge between DNA nanotechnology and Synthetic Biology as innovative biosensing approach

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Rapid and user-friendly diagnostic tests that are convenient, accessible, and well-suited for use at the point-of-care are essential for the early identification, tracking, and control of infectious diseases and other clinical needs. In this direction, in the last two decades, the advantages of synthetic nucleic acids (i.e., programmability of interactions, chemical versatility, low-cost and ease of synthesis) have been exploited by our group and many others to develop different classes of DNA-based sensors.[1] Synthetic nucleic acids are indeed highly versatile from a chemical point of view and they can be used as molecular scaffolds to conjugate different recognition elements (small molecules, proteins, etc.) and different signaling tags (optical or redox labels) thus leading to the detection of a wide range of targets, including nucleic acids, small molecules and proteins using optical and electrochemical approaches.[2] Mostly of the reported DNA-sensors provide several advantages compared to the current standard methods (i.e., immunoassays) in terms of time of measurement, cost and ease of operation convenience. However, due to the lack of a chemical or enzymatic amplification step the detection limit of these sensors is fixed by the intrinsic instrumental limitations of electrochemical or fluorescence detection and does not allow to measure the targets below nanomolar concentrations. Recently, the emerging field of synthetic biology has proposed cell-free transcription/translation biosensors as innovative analytical devices to overcome the above-mentioned limitations.[3] These systems are based on synthetic genes that can be activated in the presence of a specific target and trigger the *in-vitro* transcription of a signalling RNA strand or the translation of a signalling protein. By coupling the programmability of synthetic nucleic acids with the high sensitivity and specificity offered by the enzyme-machinery of RNA transcription, we have recently reported the first two examples of cell-free biosensors for antibodies detection.[4,5] Our approach of programming nucleic acid responsive units that can trigger the cell-free transcription of specific RNA in response to the presence of specific targets may have even broader applications than sensing. For example, we envision the possibility this strategy may be used to transcribe RNA therapeutics and to develop RNA vaccines.

References

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