Bibliographic review of Quantum Dots methods and their applications in the field of Biotechnology

Galeote Checa, Gabriel and Pimentel Naranjo, Víctor
Ingeniería de la Salud, mención en Ingeniería Biomédica, ETSII de Málaga, España.

INTRODUCTION

Quantum dots (QDs) are a novel class of inorganic fluorophore which are gaining widespread recognitionas a result of their exceptional photophysical properties. In some medical treatments QDs are very important because they provide the possibility of localise biological ultrastructures that can be seen by electron microscopy. They have great potential in the area of biological imaging and diagnostic applications because they are able to emit light in a very specific wavelength.

PROCEDURE

Fig. 1 lists conjugation schemes commonly used for attaching proteins to QDs. The properties of solubilised nanoparticles, including the charge and hydrodynamic status, will be altered depending on the method used, meaning that the solubilisation strategy will need to be tailored according to the biological system being used.

By linking QDs to proteins it can be made the labelling, for example, of F-actin fibres (*Fig. 2*). Some advantages of QDs labelling are the specific precision, photostable state and multiple colour labelling. An example of multiplexed labelling of two pathogens is shown in *Fig. 3*.

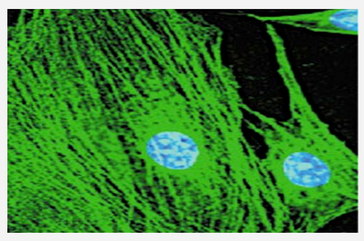

Figure 2. Actin filaments stained with a QDs composition.

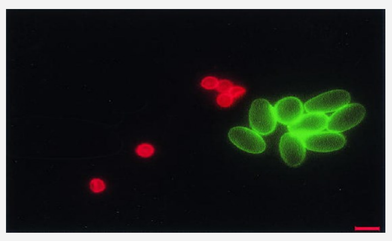

Figure 3. Simultaneous multiplexed labelling of both Cryptosporidium parvum and Giardia lamblia using immunofluorescent staining methods with QD fluorophore.

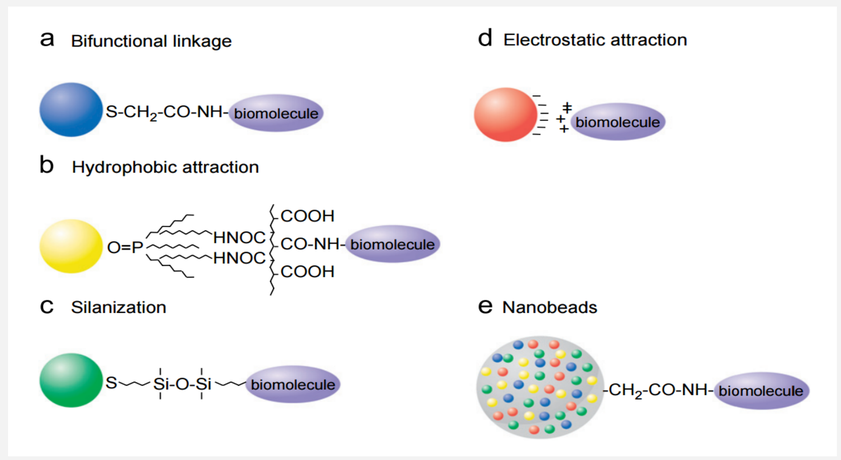

Figure 1. (a) Use a bifunctional ligand such as mercaptoacetic acid. (b) Using a modified acrylic acid polymer by hydrophobic forces. (c) Using mercaptosilane compound. (d) Positively charged biomolecules linked to negatively charged QDs by electrostatic attraction. (d) Incorporation of QDs into microbeads and nanobeads.

APPLICATIONS

Detection of pathogens and toxins, and in defining their characteristics, including virulence. For example, the application of in situ hybridisation techniques using QDs to the detection of Hepatitis B and C viruses has also been demonstrated. Using printed microarrays of sequences complementary to Hepatitis B and C virus genomes *(Fig. 4)*.

In vivo animal imaging, for studies of tumor growth *(Fig. 5 & 6)*.

Fluorescence resonance energy transfer (FRET) analysis, involves the transfer of fluorescence from a donor to a receptor and then imaging it to see the distribution of the molecules.

Gene technology, QD-conjugated oligonucleotide sequences are used to target bind DNA or mRNA.

Fluorescent labelling of cellular proteins, in this technique cells are labeled externally by QDs. Also, we can label intracellular delivery but it is more difficult because of some limitations in the cytoplasm.

Tumour Biology Investigation, tumour vasculature plays an important role in determining tumour pathophysiology, and drug delivery. Combination of QD imaging with second-harmonic generation (SHG), which has been used for collagen imaging in normal and cancer tissue has allowed imaging of the distribution of blood vessels within the interstitium, of which collagen is a major component *(Fig. 6)*.

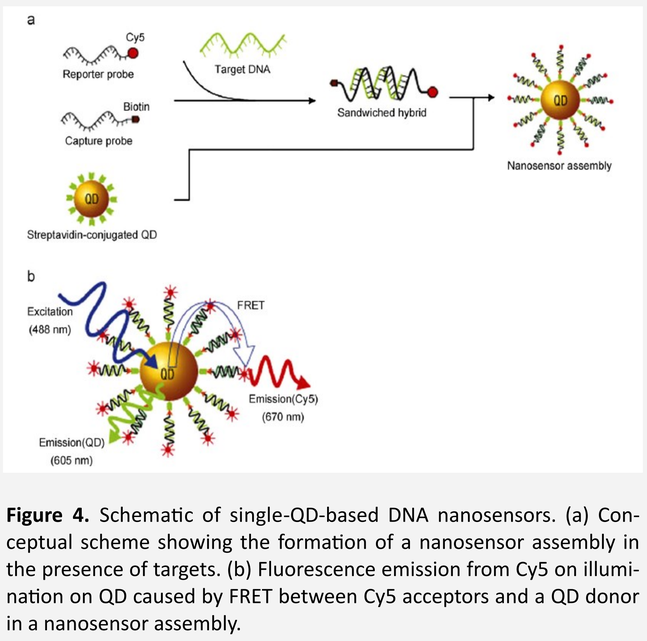

Figure 4. Schematic of single-QD-based DNA nanosensors. (a) Conceptual scheme showing the formation of a nanosensor assembly in the presence of targets. (b) Fluorescence emission from Cy5 on illumination on QD caused by FRET between Cy5 acceptors and a QD donor in a nanosensor assembly.

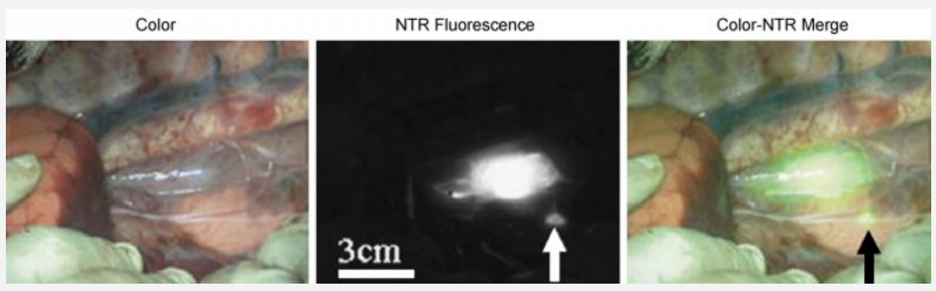

Figure 5. Esophageal sentinel lymph node mapping in pigs. Showing original colour, QD fluorescence and false-colour QD fluorescence merged with original image.

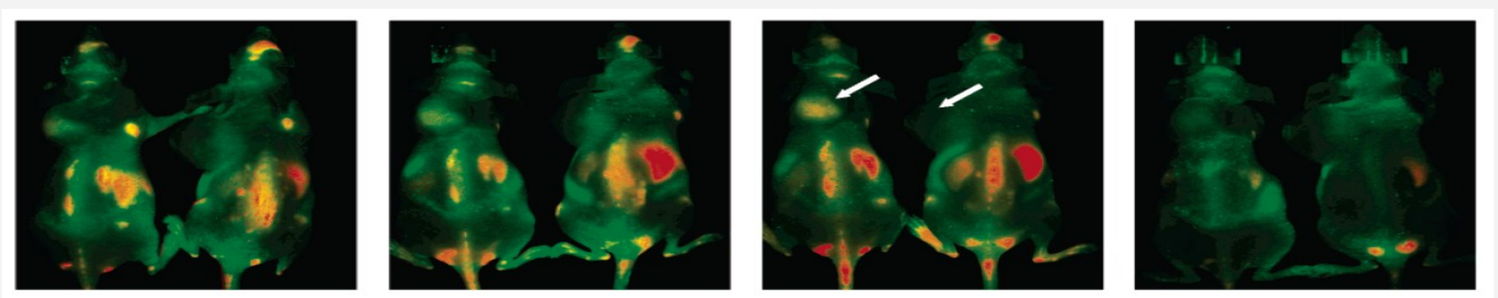

Figure 6. It can be observed how tumours have beed detected by QDs. The mice autofluorescence is color coded green while the unmixed QD signal is color coded red.

CONCLUSION

Despite the undisputable value of this new way of label is an advantage for new researches, there are some problems about the use of QDs in some medical aplications. There is evidence of cytotoxicity and alteration of cell function. Firstly, QD complexes, including their capping materials may be immunogenic, which can make a dangerous immunological response in the subject. Secondly, the core of the QDs complexes contains heavy metals which are very toxic elements for some biological organisms. Thirdly, the size of QD complexes precludes renal excretion.

However, many useful results have been generated using QDs, particularly in the field of single-molecule tracking and it can become a very useful technique to use in the future. Nevertheless, this new technique must be studied in many applications and improved before putting it on medical researches.