

APTAMERS AS MARKERS OF CELL VIABILITY IN REGENERATIVE MEDICINE

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LATTICE BIOLOGICS IS USING APTAMER TECHNOLOGY TO DEVELOP NEXT GENERATION ALLOGRAFTS TO:

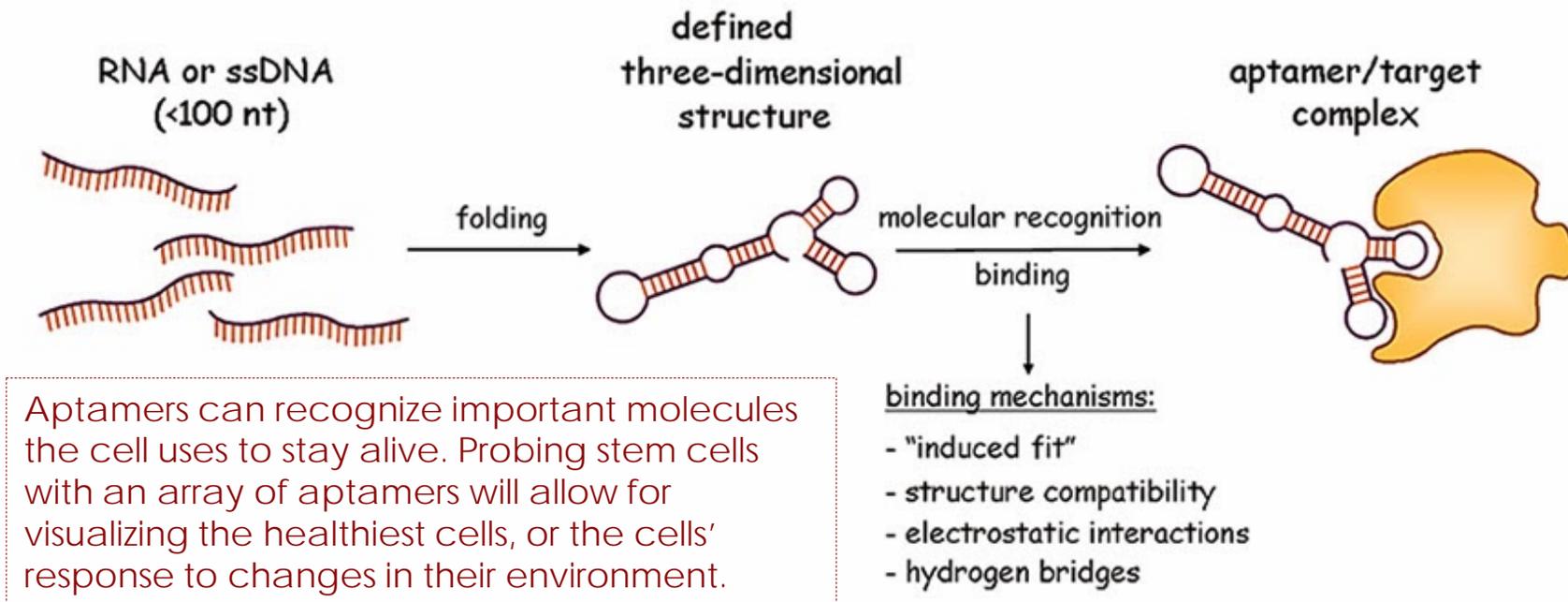
1. Tap into the body's ability to heal itself and regenerate
2. Provide accelerated healing times
3. Harness the power of stem cell technologies

Part of this process involves identifying new ways to understand human biology, down to the cellular and even the molecular level. Powerful new analytical tools are emerging and being adopted for purposes of bioengineering. One such tool is the use of fluorescence microscopy which, in conjunction with constructed fluorescent compounds such as aptamers, will enable the monitoring of the specific environment a living cell endures. The ability to image and measure elements of the healing environment encountered by a regenerative stem cell population is invaluable for tailoring medical devices and therapies to achieve better patient outcomes.

Aptamer technology is a key that will take regenerative medicine in new directions... leading to our goal of providing stronger and more efficient surgical and therapeutic solutions.

ABOUT APTAMERS

Definition: The word "aptamer" is derived from the Latin term, *aptus*, meaning "fit" and the Greek word, *meros*, meaning "part."



Aptamers are small polymers (in this case, made from DNA or RNA) that bind other biological molecules strongly and specifically, because of their ability to fold into 3-dimensional "custom-fit" structures.

Figure credit: <http://www.technologyinscience.blogspot.com>

ADVANTAGES OF APTAMERS

Aptamers offer one of the best solutions for concisely assessing the status of stem cells. Traditional technologies have shortcomings when it comes to addressing this challenge.

How aptamers are superior to existing technologies:

1. Capable of greater specificity and affinity than antibodies, yet are more stable at ambient temperatures.
2. Easily modified chemically to yield improved, custom tailored properties.
3. Can be used on living cells for a more accurate “snapshot” of the health of the cells, as opposed to existing methods that involve killing the cells and separating their components.
4. Customizable and suited for diagnostics.

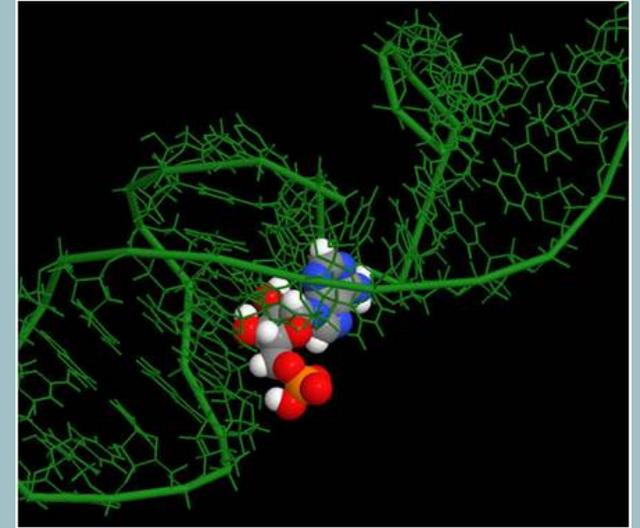


Figure: Aptamer (green) binds the cellular energy metabolite ATP

BUILDING THE APTAMER TOOLKIT

Aptamers not only bind objects, but also report back. Aptamers have been engineered to emit colors of light when they have found their target molecules. The intensity of the light emitted from this “fluorescent reporter complex” is indicative of the abundance of the target molecule. This allows true measurements to be made of the metabolic activity inside of cells - information that denotes the health of those cells.

Various engineering approaches have enabled strategic aptamer modifications:

1. to be fluorescent upon binding their target.
2. to distinguish raw materials from end-products in certain metabolic pathways.
3. to act as “molecular beacons” that give a readout of a cell’s viability.

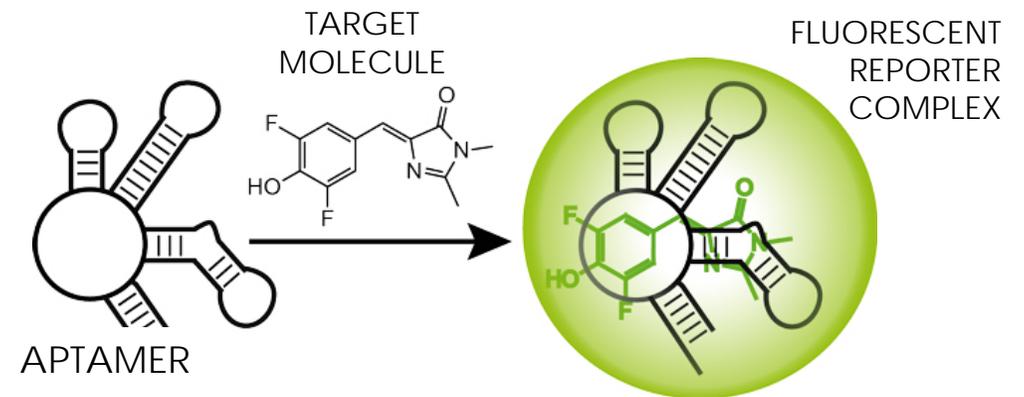
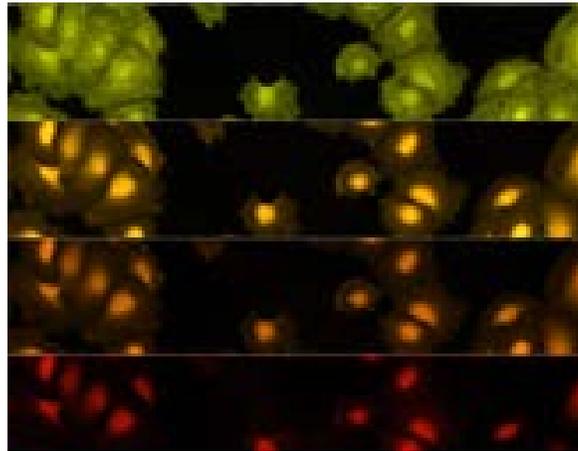


Figure credit: <http://metarna.eu/science-and-projects/rna-based-projects>

APTAMERS - TOOLS FOR ASSESSING CELLULAR HEALTH

Multicolored aptamers that recognize different cellular metabolites can indicate whether stem cells are suitable for use. Since metabolites from different biochemical pathways can be measured in living cells, environmental conditions can be optimized for those most conducive to stem cell health (viability).



energy metabolites: **ATP** → **ADP**

a high yellow-green ratio could indicate optimal energy balance in stem cells

redox metabolites: **GSSG** → **GSSH**

a high orange-red ratio could indicate cells are "primed" for transplantation

The capacity to simultaneously monitor the ratios of metabolites in live cells provides an immensely **powerful diagnostic tool** for use in regenerative medicine and stem cell therapies.

Figure modified from: <http://www.photonics.com/m/Article.aspx?PID=6&VID=124&IID=830&Tag=Products&AID=57594>

APTAMERS - APPLICATIONS FOR STEM CELL THERAPIES

Fluorescent aptamers used as cell viability markers can:

1. Distinguish the fraction of stem cells that are most regenerative.
2. Elucidate stem cell responsiveness to changing growth conditions.
3. Increase the success of stem cell transplantation and healing outcomes.

Many stem cell therapies could benefit from the combined approach of using fluorescent multi-color aptamers that illuminate and direct the healing process.



Figure credit: Gemma Estrada Girona and Petra Riedinger, EMBL