Literature report Ⅳ

nature chemistry

ARTICLES

https://doi.org/10.1038/s41557-020-0506-4

Check for updates

Single-molecule visualization of DNA G-quadruplex formation in live cells

Marco Di Antonio[1,2,7], Aleks Ponjavic[1,3,4,7], Antanas Radzevičius[1,7], Rohan T. Ranasinghe[1], Marco Catalano[1], Xiaoyun Zhang[1], Jiazhen Shen[5], Lisa-Maria Needham[1], Steven F. Lee[1], David Klenerman[1] and Shankar Balasubramanian[1,5,6]

Reporter: Jin Li

Date: 2020-07-30

David Klenerman

The Klenerman Lab

Watching single molecules in action.

Focus on developing and applying biophysical methods to biological and biomedical problems

Shankar Balasubramanian

Research:

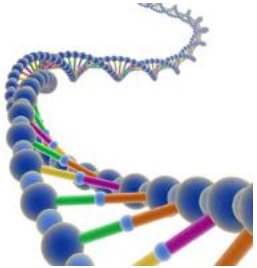
- The first is structures that form in DNA and RNA with an emphasis on G-quadruplexes.
- The second is chemically modified bases in DNA.

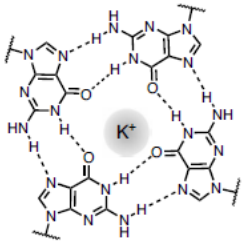
The Balasubramanian Group

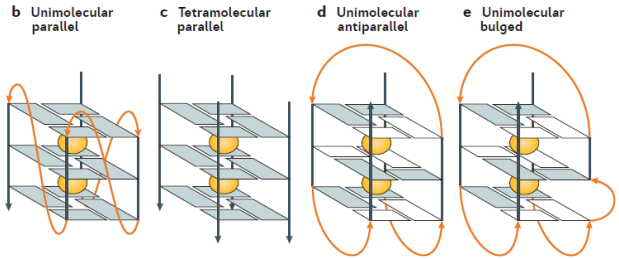
Commercial technology:

- decoding DNA called Solexa-Illumina sequencing, With David Klenerman
- chemistry for decoding epigenetic and other modified bases in DNA, commercialised via Cambridge Epigenetix

G4s

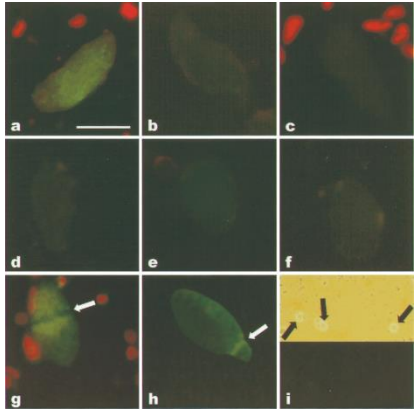




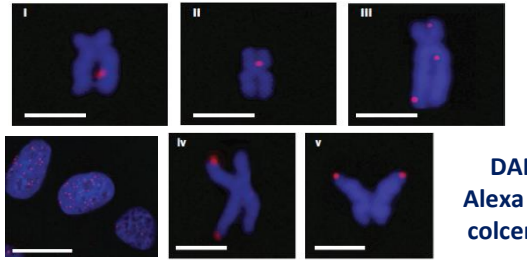


Nat. Rev. Mol. Cell Biol. **2017**, 18, 279

Nature **1988**, 334, 364–366



Proc. Natl Acad. Sci. USA **2001**, 98, 8572



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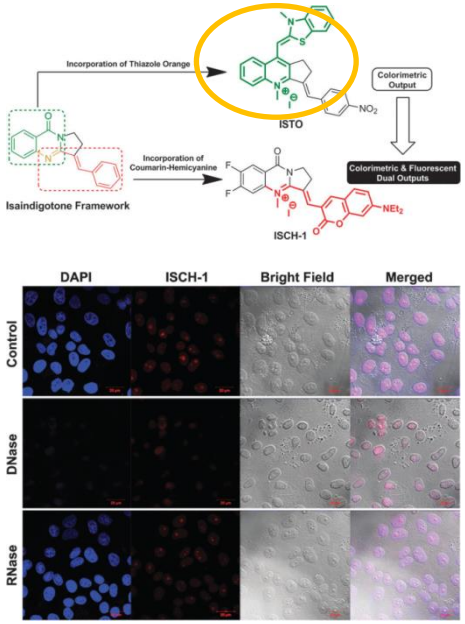
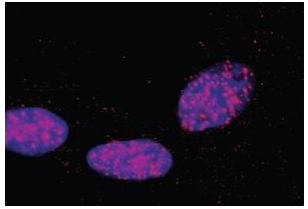
colcemid

Nat. Chem. **2013**, 3, 182

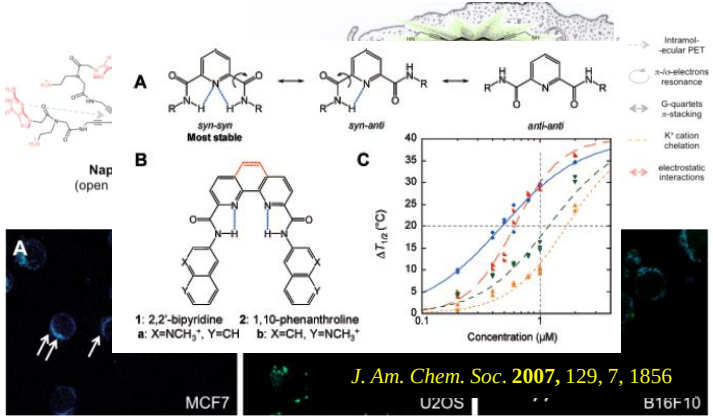
RNA G4s



Chem. Commun., **2014,50**, 6927

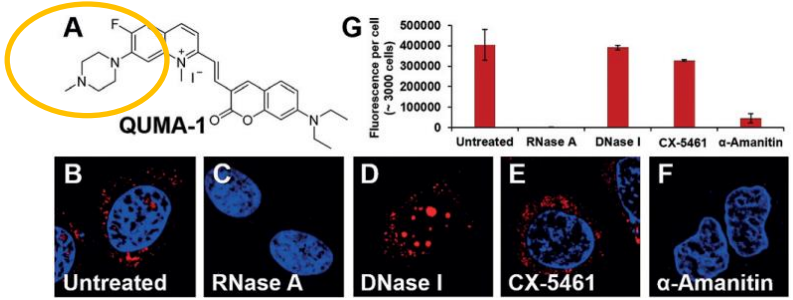


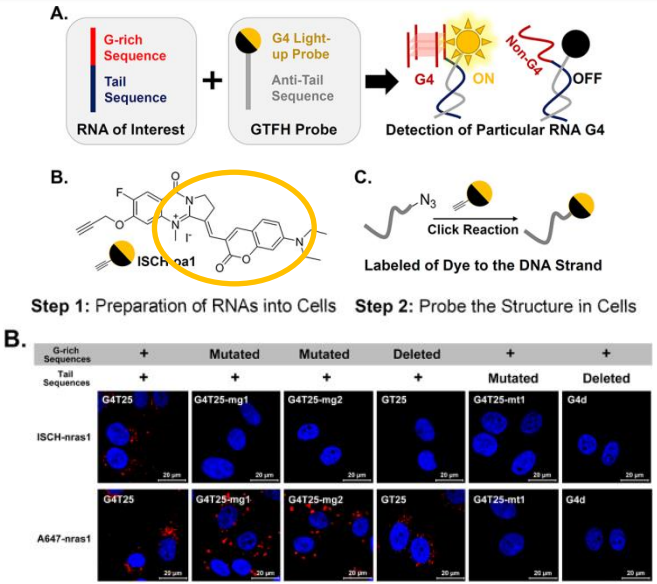
Nat. Chem. **2014**, 6, 75



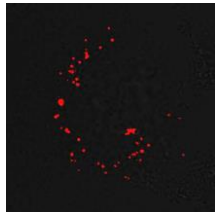
J. Am. Chem. Soc. **2007,** 129, 7, 1856

J. Am. Chem. Soc. **2015**, 137, 8521



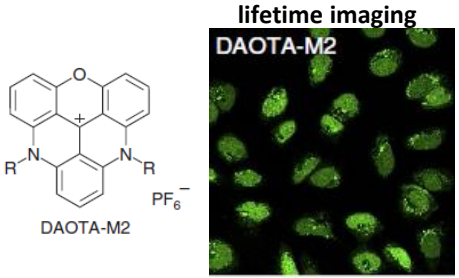


J. Am. Chem. Soc. **2016**, 138, 33, 10382

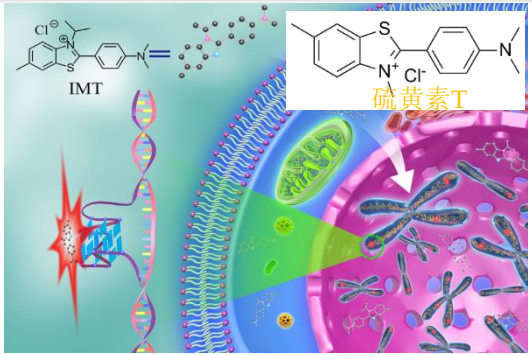


Angew. Chem. Int. Ed. **2018**, 57, 4702

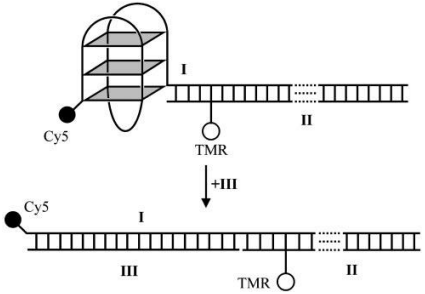
DNA G4s



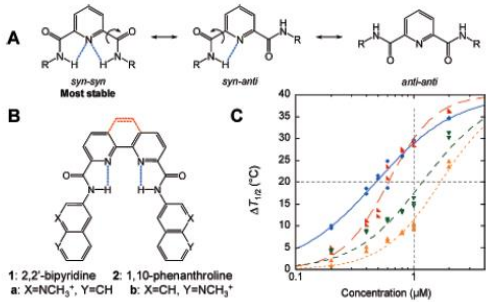
Nat. Commun. **2015**, 6, 8178



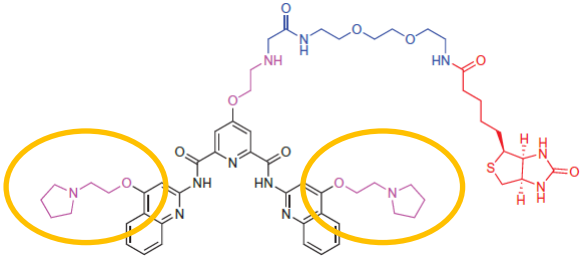
Nucleic Acids Research, **2018**, 46, 7522



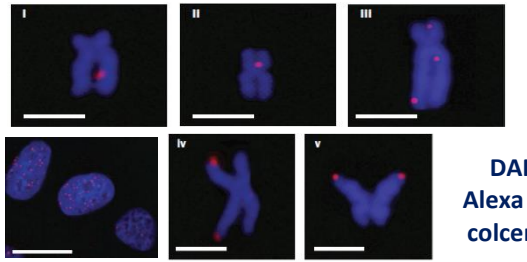
Proc. Natl Acad. Sci. USA. **2003**, 100, 14629



J. Am. Chem. Soc. **2007,** 129, 7, 1856



Nature Chem., **2010**, 2, 1095



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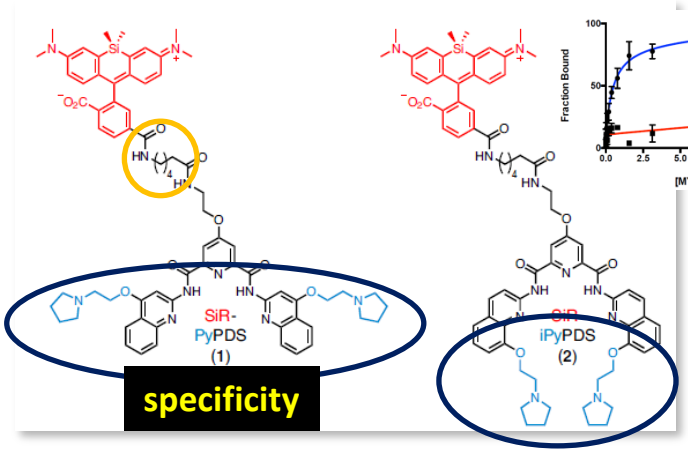
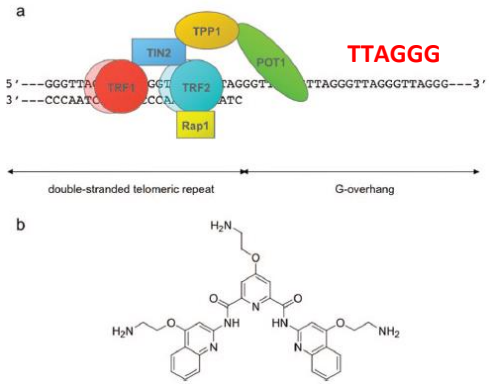
Nat. Chem. **2013**, 3, 182

The fluorescent G4 probe SiR-PyPDS

J. Am. Chem. Soc. **2008**, 130,15758





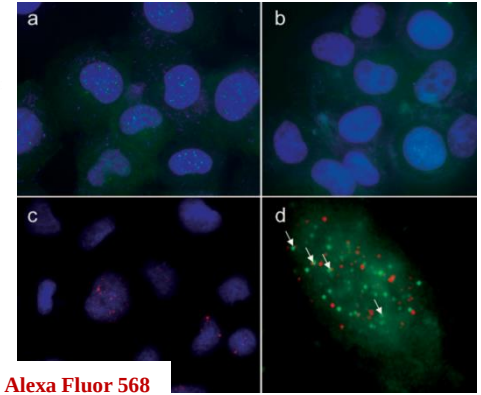
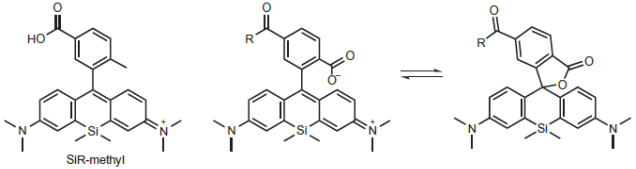
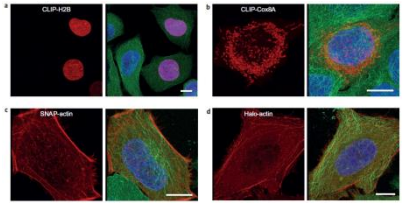
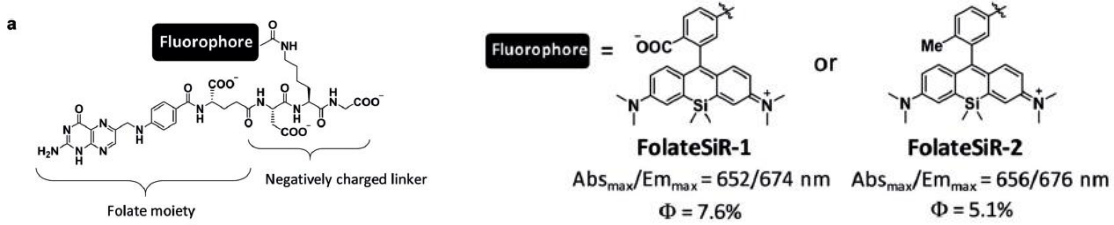


Fig. Effect of compound on HT1080GFP-POT1 cells: (a) Untreated control, fluorescent GFP-POT1 (green); (b) after treatment with 1 (1 μM) for 72 h; (c) γH2AX foci in cells treated with 1 (3 μM) for 24 h (red); (d)colocalization of γH2AX foci (red) and GFP-POT1 (green) at telomeres (marked with arrowheads). DAPI DNA staining (blue) throughout





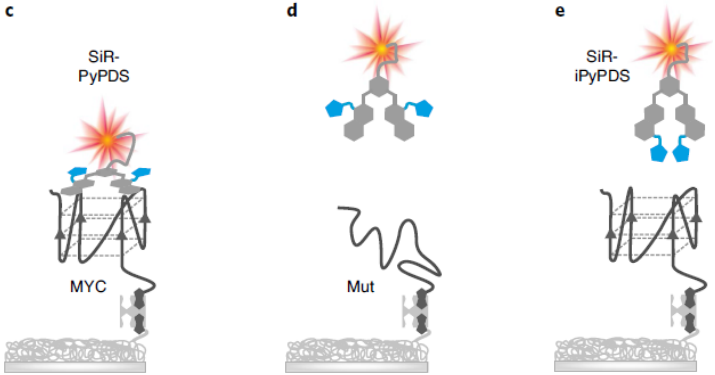
Kai Johnsson, *Nat. Chem.* **2013**, 5, 132

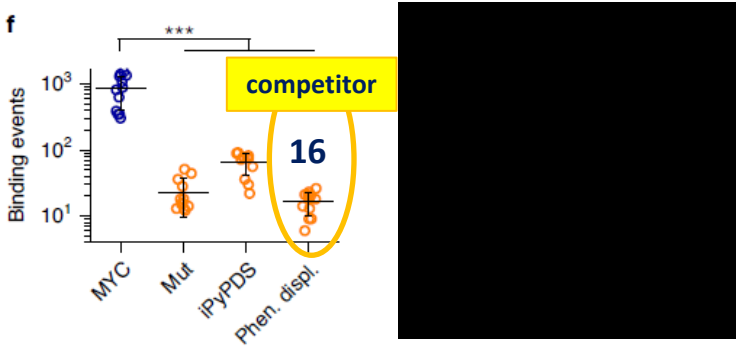


Angew. Chem. Int. Ed. **2020**, 59, 6015

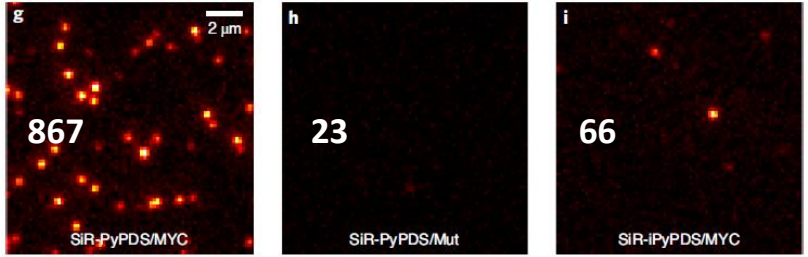
In vitro single-molecule fluorescence imaging of G4s

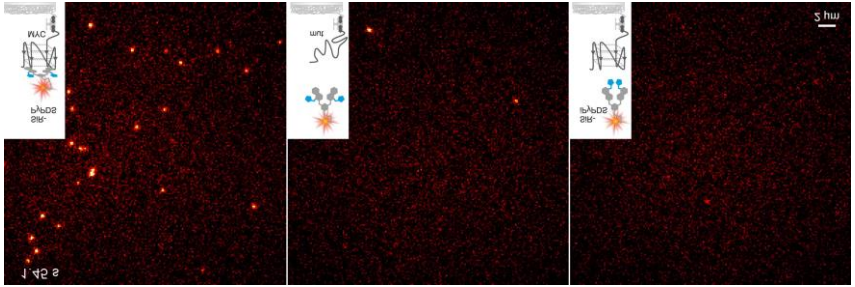
~0.05%



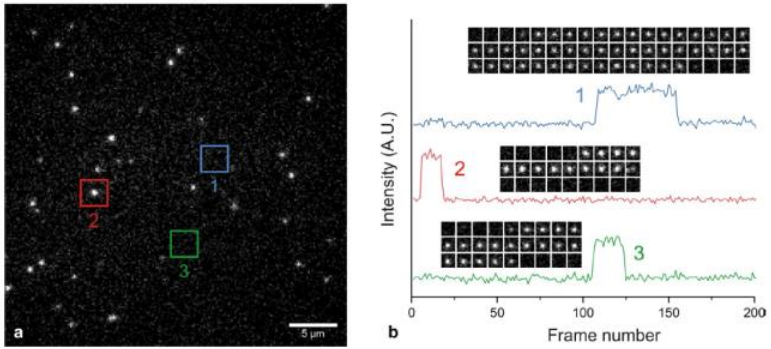


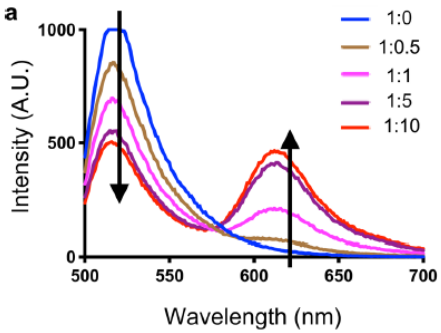
exposure time of 500 ms, 250 pM

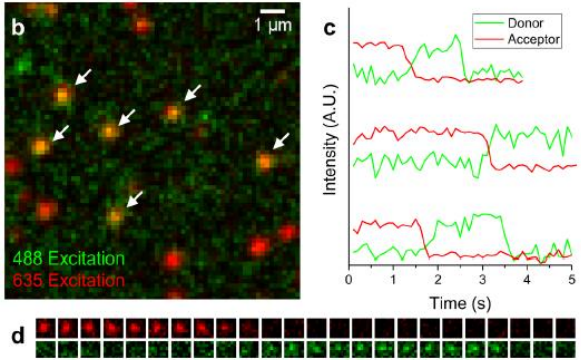


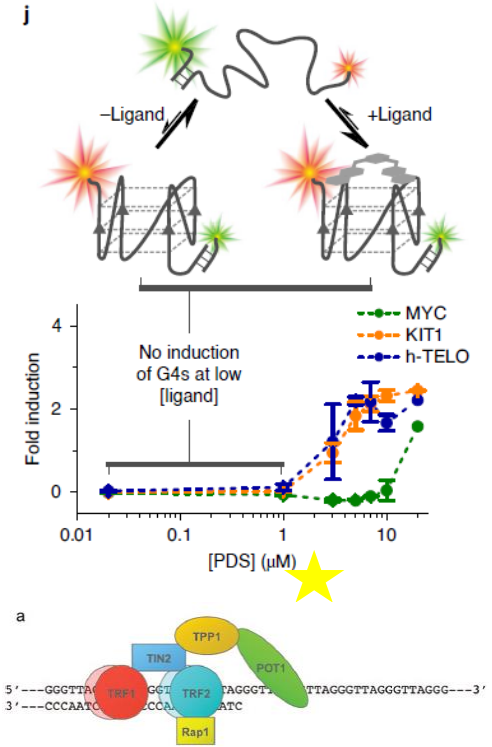


In vitro single-molecule fluorescence imaging of G4s

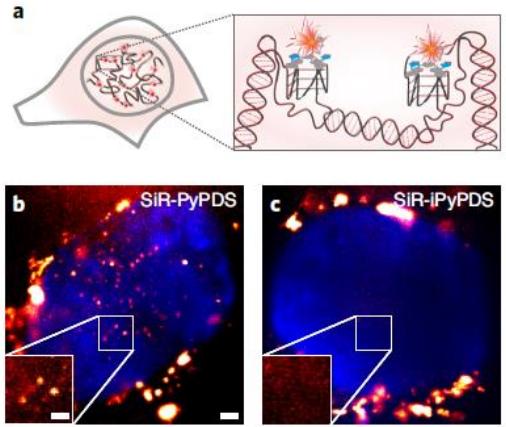


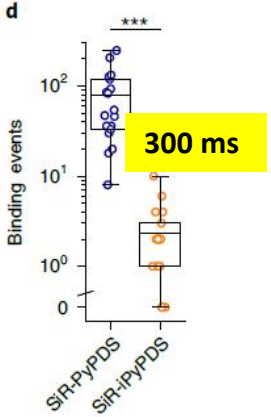


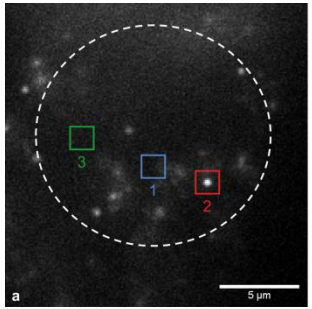


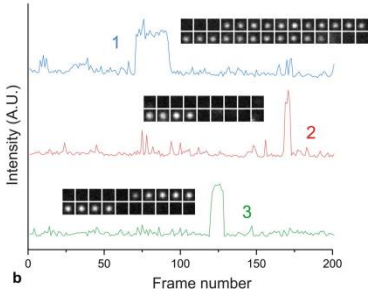


Single-molecule fluorescence imaging of G4s in living cells using the fluorescent probe SiR-PyPDS (1) ~0.4%









exposure time of 100 ms

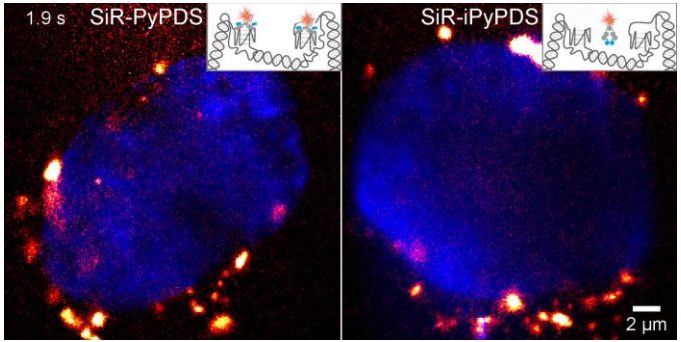
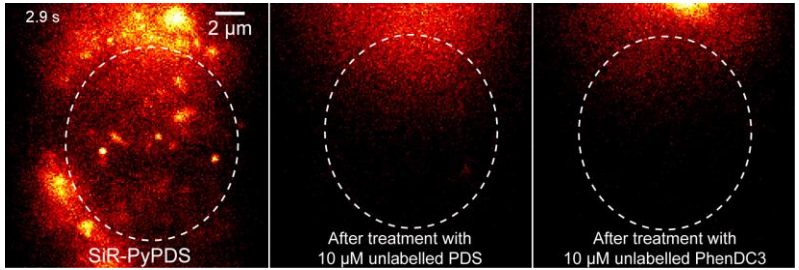
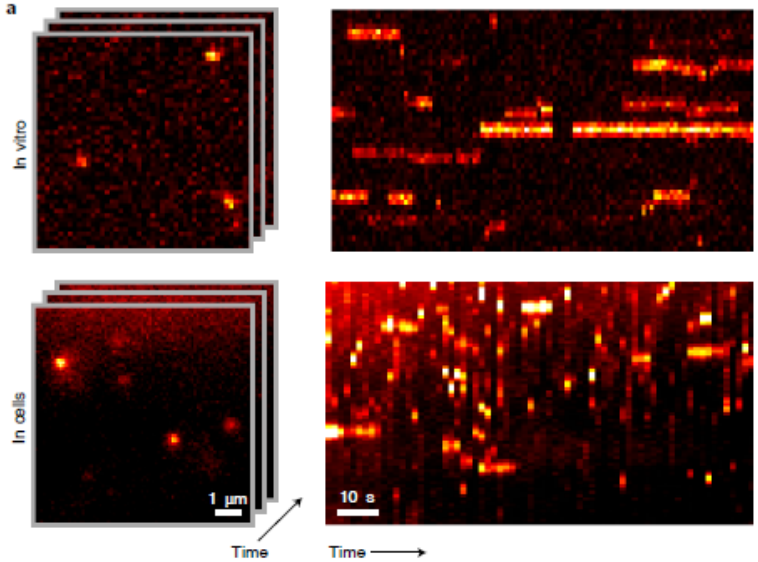
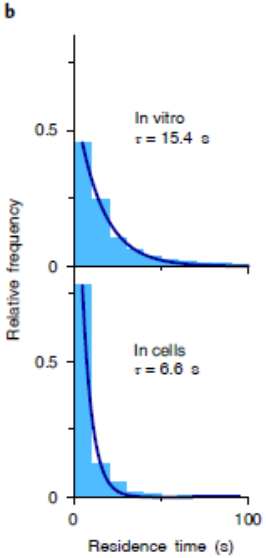


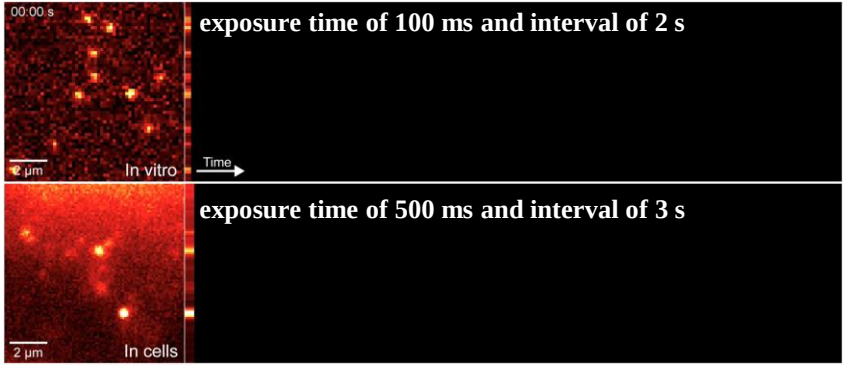
Fig. U2OS cell
treated with 20 nM
for 30 min before imaging
nuclear staining with Hoechst 33342

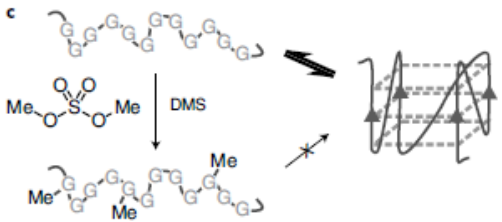


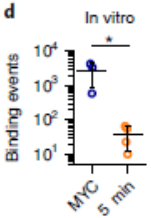
G4s in living cells undergo dynamic folding and unfolding

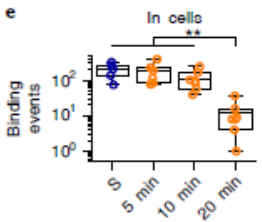


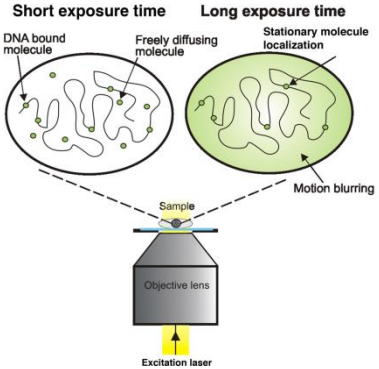


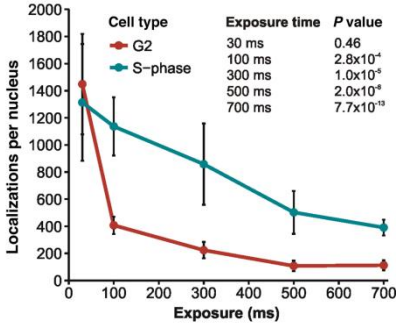






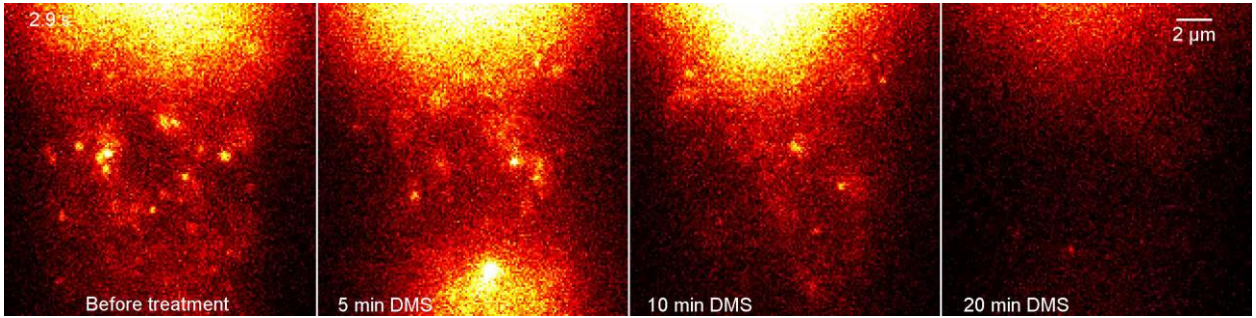




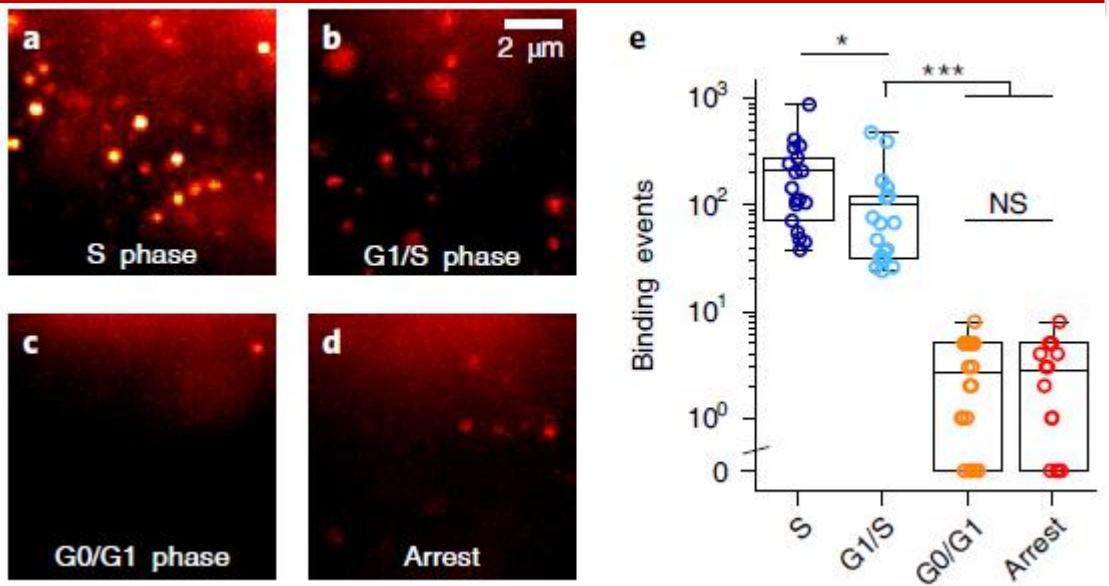


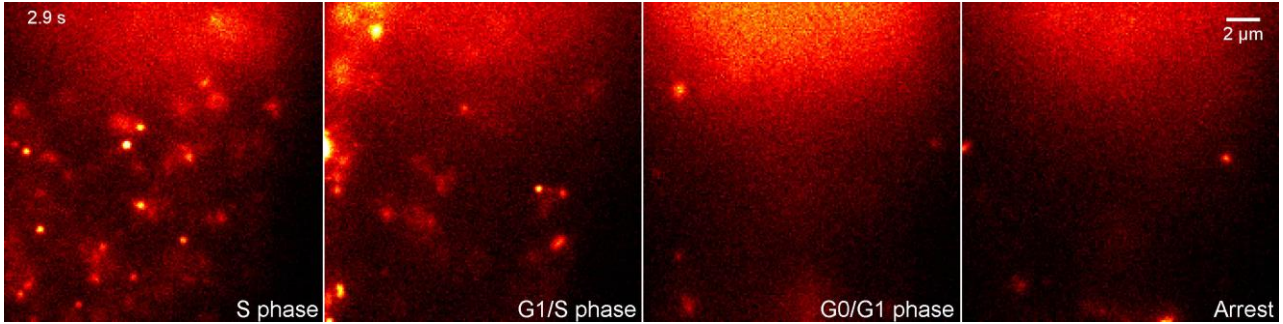
Nucleic Acids Research, **2014**, 42, 1

G4s in living cells undergo dynamic folding and unfolding



The observation of G4s in live cells is altered by cell-cycle phase and transcription





Thanks for your attention!