Nanopore–Facilitated Single Molecule Detection of Circulating MicroRNAs in Cancer Patients

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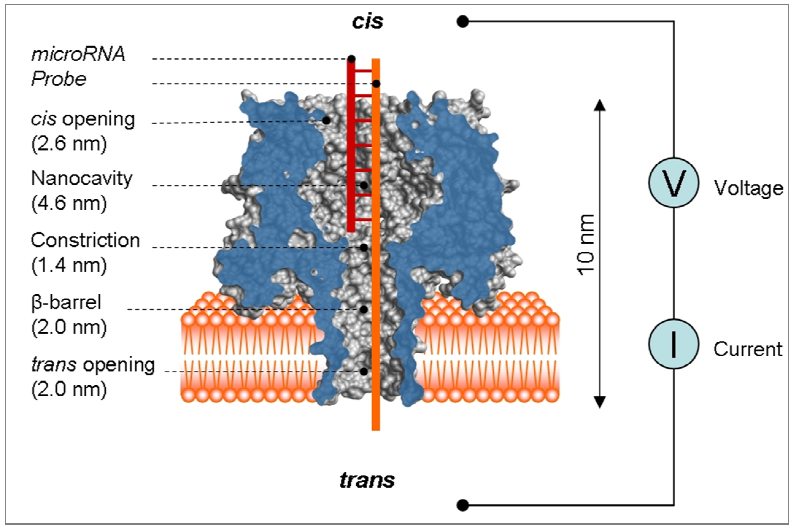
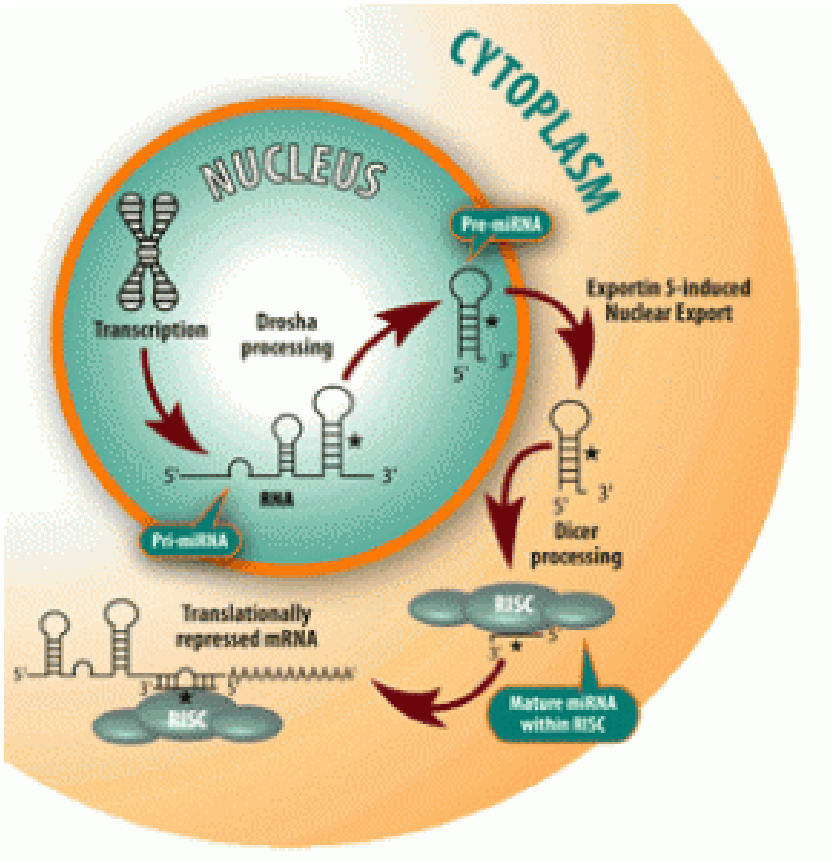
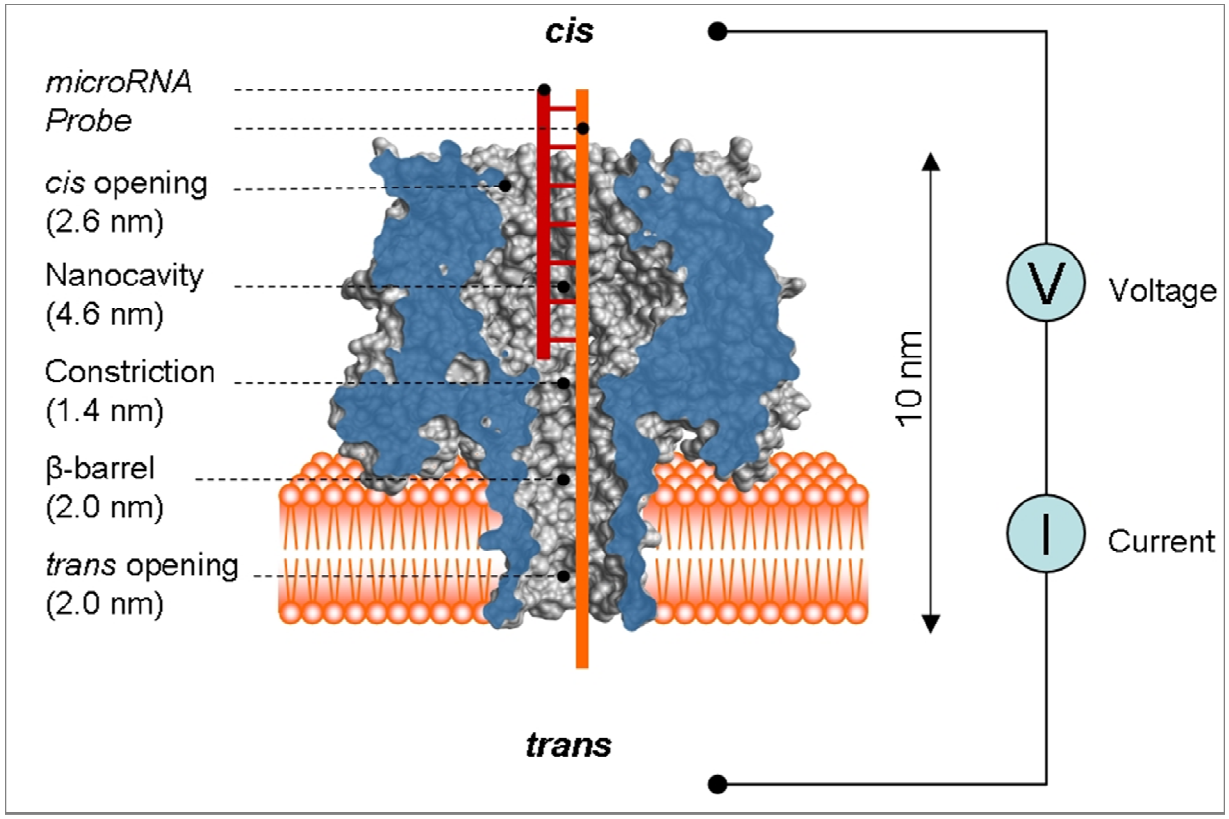


MicroRNAs as potential biomarkers for cancer detection

- MicroRNA (miRNAs): short (~18-24-nt) non-coding RNAs molecules that regulate gene expression at the post-transcriptional level.
- Aberrant expression of miRNAs has been found in all types of tumors, thus miRNAs have been recognized as potential cancer biomarkers.
- Most notably, specific miRNAs are released from the primary tumor into blood circulation, making the detection of circulating miRNAs profile a powerful tool for noninvasive cancer detection, diagnosis, staging, and monitoring.

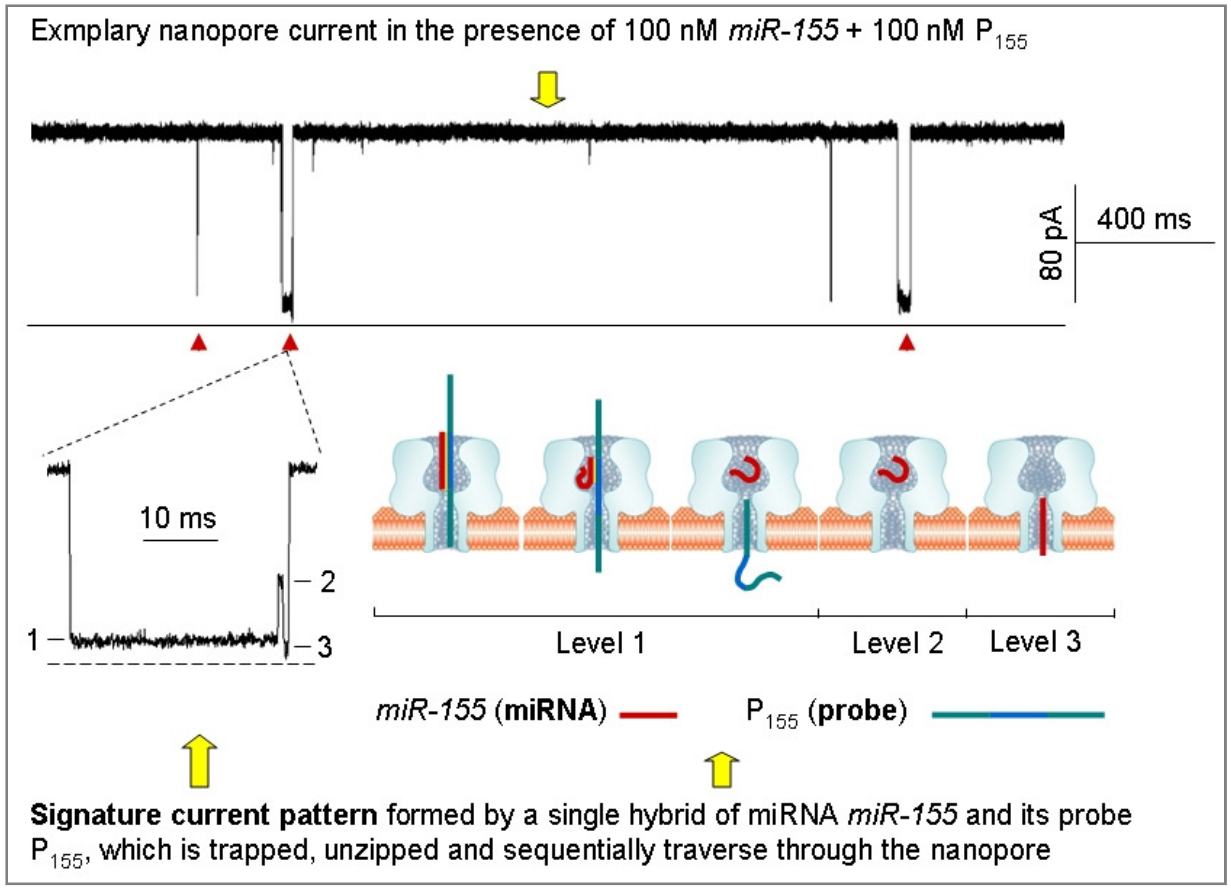


Nanopore sensor for microRNA detection



The nanopore is a fabricated 2-nm molecular pore. We developed a robust Nanopore Sensor that selectively detects single molecules of circulating miRNAs derived from primary cancer.

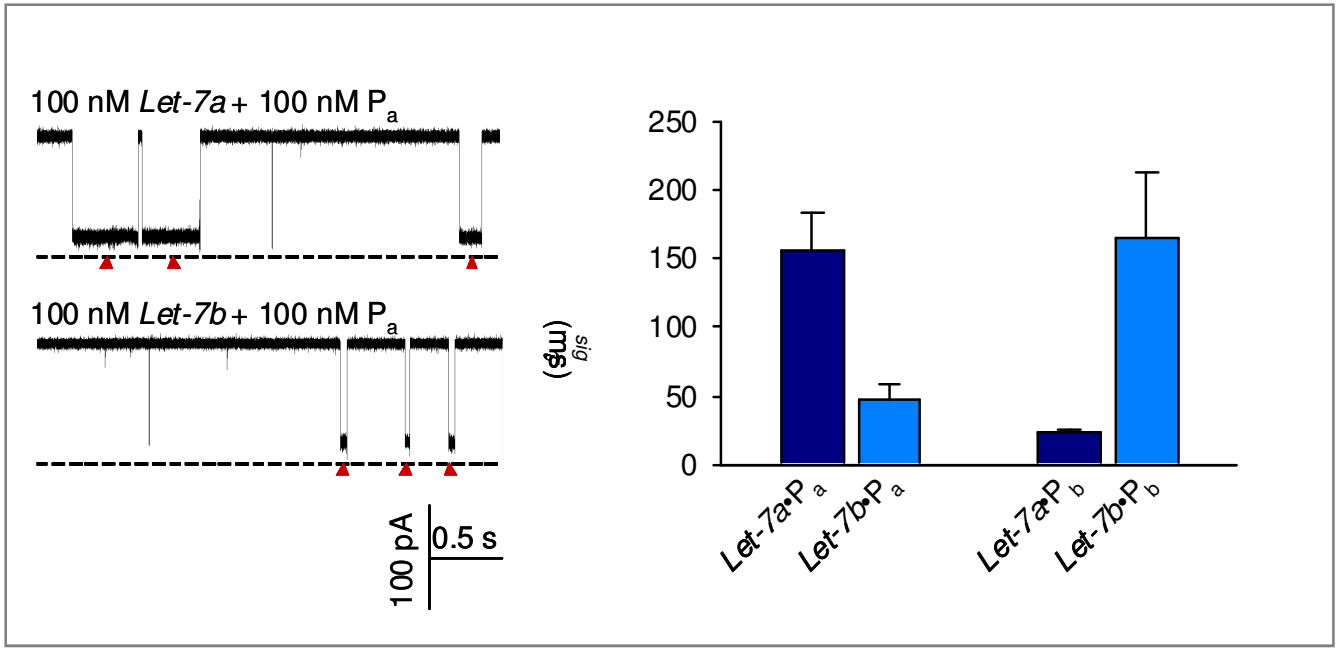
Generating signature signal for single miRNA molecules identification



Signature current pattern formed by a single hybrid of miRNA *miR-155* and its probe P_{155}, which is trapped, unzipped and sequentially traverse through the nanopore

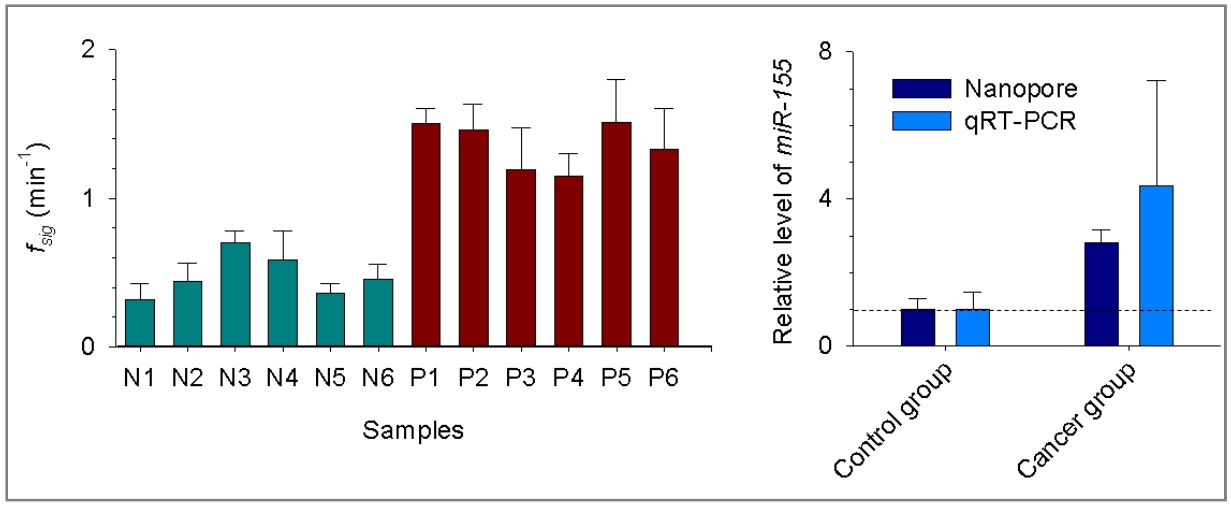
Such a tiny pore can generate a signature current signal when a miRNA molecule is specifically captured in it. These signals function as fingerprints that enable us to identify a specific miRNA and quantify its concentration.

Discrimination of single nucleotide difference between two miRNA molecules



The prototype of nanopore sensor has demonstrated the capability to discriminate single nucleotide difference between miRNAs, i.e. single nucleotide polymorphisms (SNPs).

Detection of *miR-155* in lung cancer patients' plasma.



In clinical tests, the nanopore has shown the power to differentiate miRNA levels in blood from lung cancer patients and healthy people.

Advantages over the gold standard RT-PCR and microarray

1. label-free;
2. no need of nucleic acids amplification
3. single molecule detection ensures higher selective, precise and accurate over the gold standard RT-PCR and microarray;
4. noninvasive clinical test;
5. requires a mere 5 ml of peripheral blood
6. reduced cost from several hundred dollars today to less than 20 dollars per sample, 7. The developing nanopore array gives a high throughput capability for detecting miRNA profile.
7. If validated in clinical trial, the nanopore sensor will become a system available to monitor cancer patients and to screen high risk populations for early diagnosis of cancers which will potentially save the lives of millions.