

## How microfluidics ultrahigh-throughput screening enables the discovery of aptamers enzyme inhibitors.

Based on the work of Michaël Ryckelynck “Digital Biology of RNA” Research team from IBMC.

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Microfluidics consists in manipulating of microliters to picoliters volumes of fluid in lab-on-chip devices, allowing to miniaturize and automate biological assays<sup>1</sup>. Aptamers are single-stranded nucleic acids adopting a 3D structure conferring them the capacity to specifically interact with a target like a protein<sup>2,3</sup>. Aptamers have similar uses to antibodies, but antibodies development takes a long time and requires *in vivo* screening, whereas, aptamers can be developed *in vitro*, using ultrahigh-throughput methods. The “*Digital Biology of RNA*” research team of IBMC used *SELEX* and  $\mu$ *IVC-seq* methods together with bioinformatics to find out an aptamer that specifically inhibits the *SPM-1* enzyme. This enzyme degrades several antibiotics and provides drug-resistance to strain expressing it. A specific inhibitory aptamer of *SPM-1* could resensitize *SPM-1* expressing strains to the antibiotic. The *SELEX* method isolates *SPM-1* ligand aptamers sequences from  $10^{15}$  sequences randomly generated. Then, the  $\mu$ *IVC-seq* method is used to select *SPM-1* inhibitor aptamers from *SPM-1* ligand aptamers. The specific *SPM-1* inhibitor aptamers are then sequenced, to identify them and model their 3D structure. In addition, the aptamers were tested for RNase resistance and to be functional in a medium reproducing physiological ionic concentration. Microfluidic screening enables ultra-specific molecules to be selected rapidly and economically, thanks to the miniaturization of samples and automation of processes<sup>3</sup>.

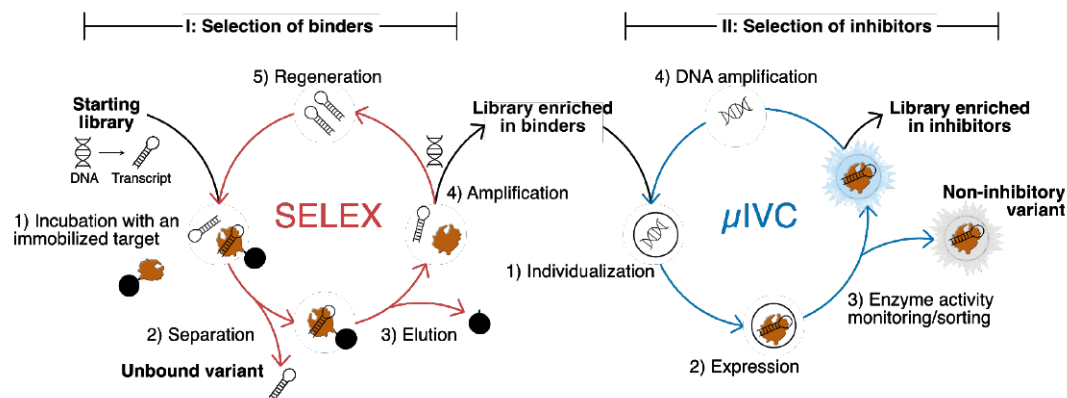


Figure: Ultrahigh-throughput microfluidic screening using *SELEX* and  $\mu$ *IVC-seq* methods<sup>3</sup>.

### References

1. Chou, W.-L., Lee, P.-Y., Yang, C.-L., Huang, W.-Y. & Lin, Y.-S. Recent Advances in Applications of Droplet Microfluidics. *Micromachines* **6**, 1249–1271 (2015).
2. Kehrlı, J., Husser, C. & Ryckelynck, M. Fluorogenic RNA-Based Biosensors of Small Molecules: Current Developments, Uses, and Perspectives. *Biosensors* **14**, 376 (2024).
3. Husser, C. *et al.* Ultrahigh-throughput discovery of modified aptamers as specific and potent enzyme inhibitors. Preprint at <https://doi.org/10.1101/2024.08.16.608213> (2024).