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MES
Molecular & Experimental Surgery

CRISPR/Cas-based liquid-biopsy diagnostics for rapid and sensitive monitoring of cancer treatment response

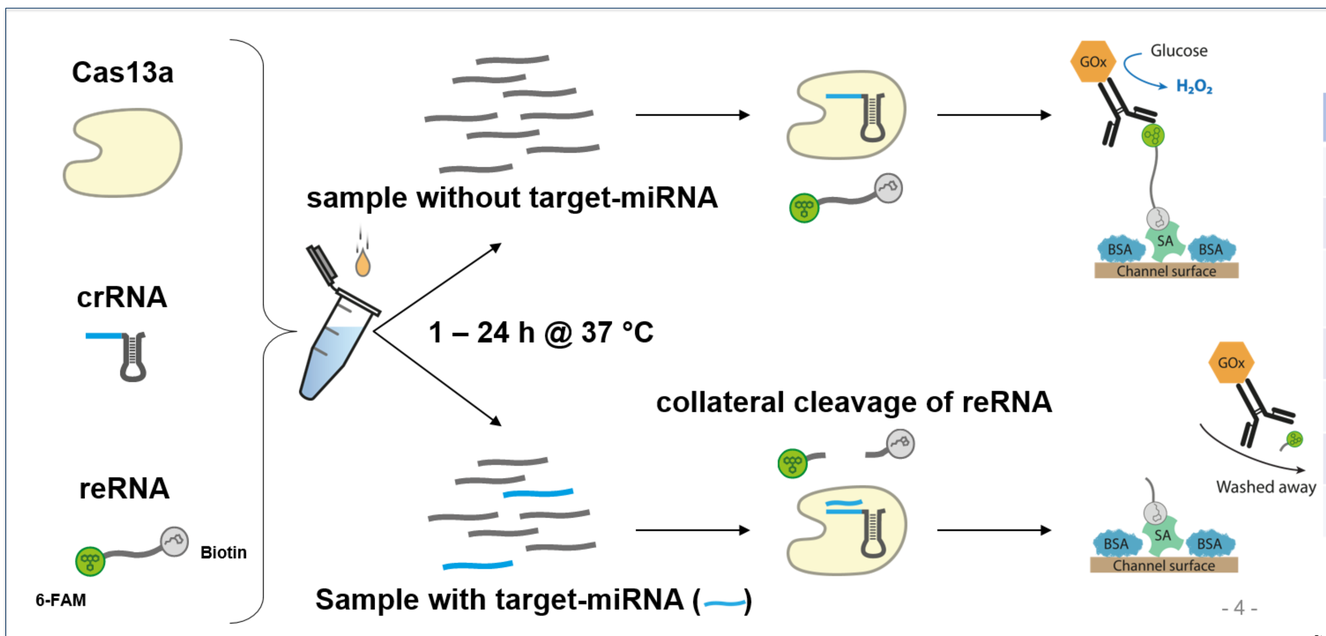
Background:

- Cancer patients suffer from inevitable uncertainty whether the applied treatment regimes result in sufficient tumor control
- Current clinical diagnostics mostly relay on socialized instruments, that purchase, maintenance and application are highly cost intensive and sometimes even result in uncertain results (pseudoprogression)
- Nucleic acid fragments generated by the cancer cells in the micro environment has been described in various preclinical and clinical context
- Utilizing the nucleic acid sheddome of cancer cells reaching the blood stream – in the free fraction or embedded in vesicles - emerges as innovative approach in cancer diagnostics
- Current clinical nucleic acid diagnostics requires target amplification causing delay in results determination, and limitations in minimal detection threshold and specificity

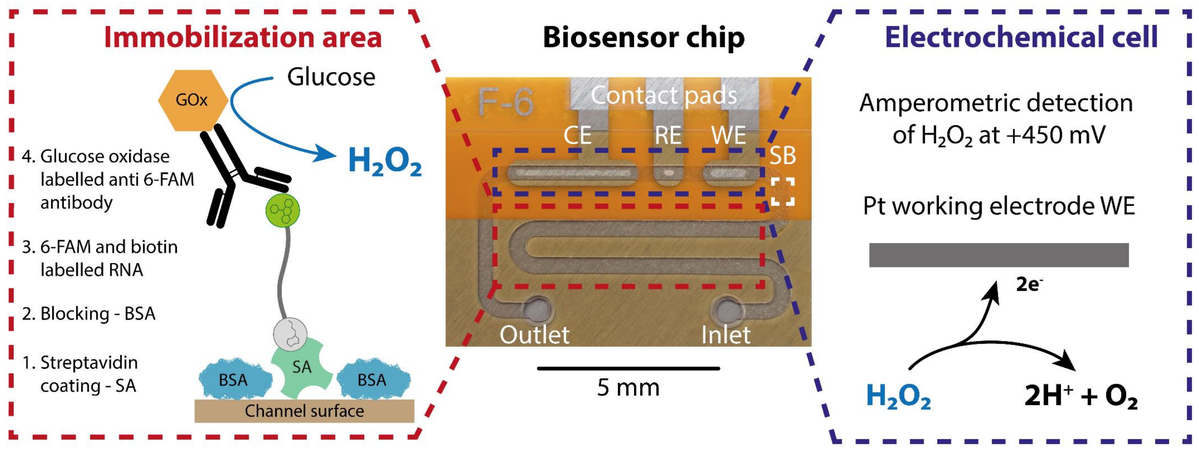
Aims:

- Development of a multiplex, application-free blood test chip to detect cancer recurrence focusing on candidate microRNAs positively regulating cancer stem cells

Translational pipeline:



Parameter	CRISPR/Cas Biosensor	qPCR
flexibility	Simple to adjust → crRNA	specific primers and optimization
reverse transcription	no	yes
Time to result	~ 4 h	~ 6.5 h
Hands-on-time	~ 30 min	~ 2.0 h
costs	Ultra low, disposable	medium
Sample usage	Ultra low	medium
Handling	Minimal trained staff	Lab technician level



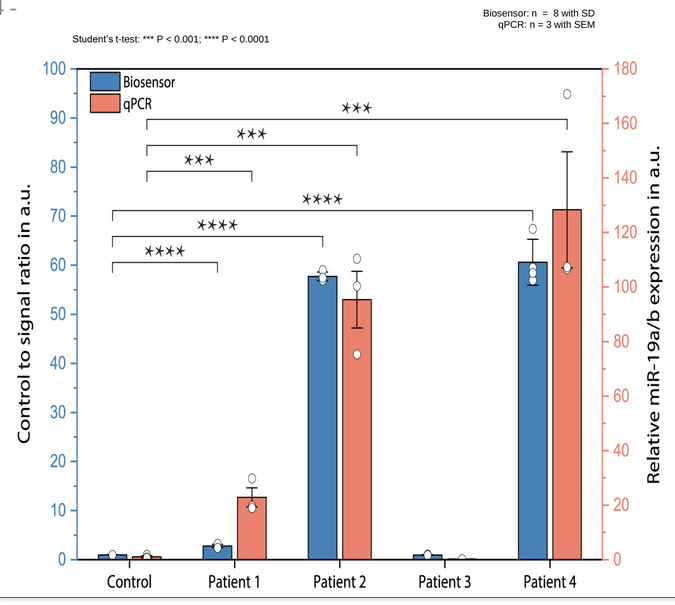


Fig1: Principle pf the basic biochemical background and layout of the first version of the electrochemical CRSIPR sensor for rapid, resource efficient, sensitive (low pM range) target detection, comparison to gold standard assay PCR

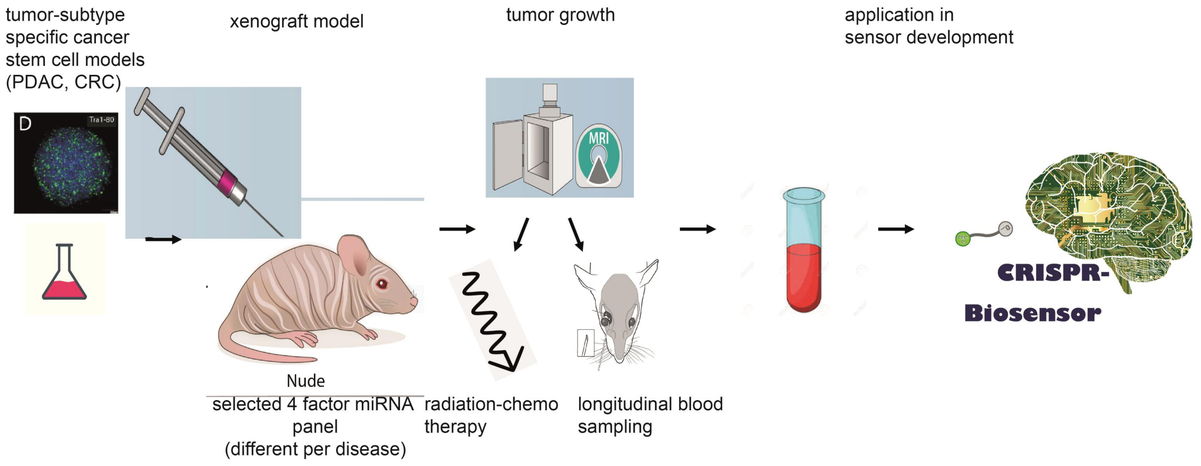


Fig2: Sensor development towards tumor stem cell multiplex miRNA panel

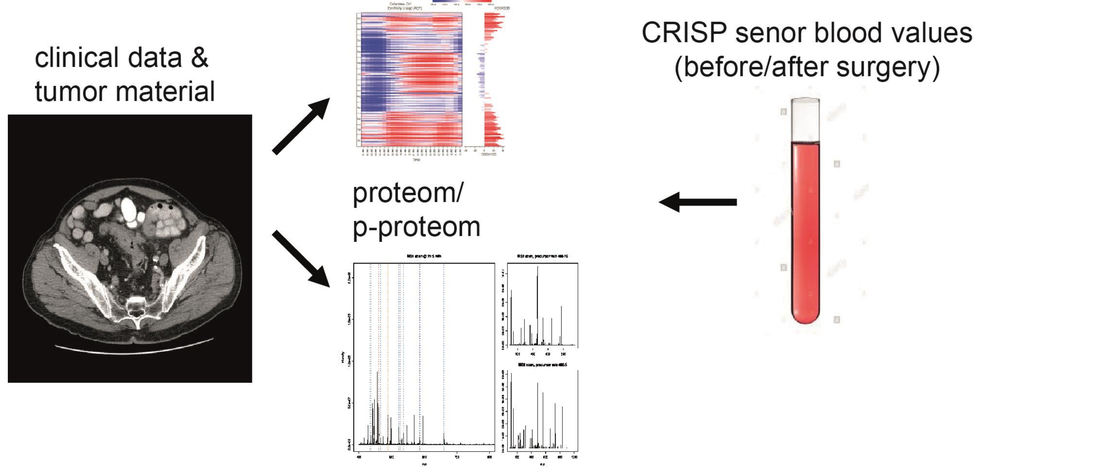


Fig3: An elevated COL10A1 expression is significantly associated to CAFs consensus signature and to altered immune checkpoint expression levels

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References:

[1] Bruch et al., 2019; [2] Ates et al., 2020