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Sequencing By Binding (SBB) Shows Superior Sensitivity and Specificity of Detection of Low Frequency Variants from ctDNA

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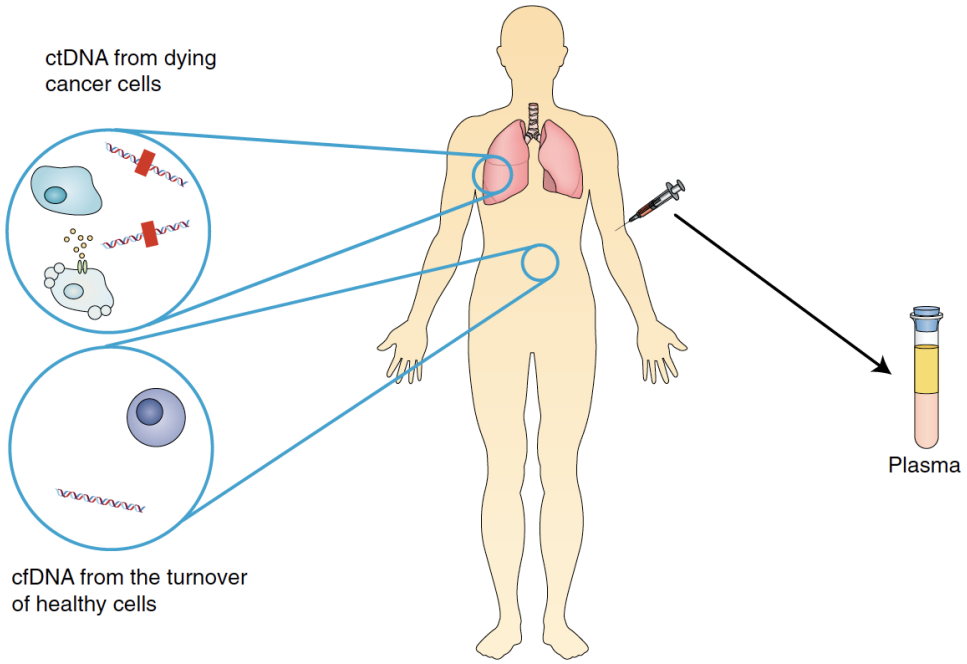
Liquid biopsies and the challenges of ”needle in a haystack”

Only a small fraction of cell-free DNA (cfDNA) is circulation tumor DNA (ctDNA)



Song et al, Nature Biomed Engineering, 2021

Amount of cfDNA shed by solid tumors depends on cancer stage and tumor size

Tumor diameter	Number of genomes per 10ml of blood	Likelihood of detection by ctDNA
27mm	6	High
12.5mm	~1	Moderate/Low
6mm	<<1	Unlikely

Improve the sequencing Sequencing By Binding (SBB)

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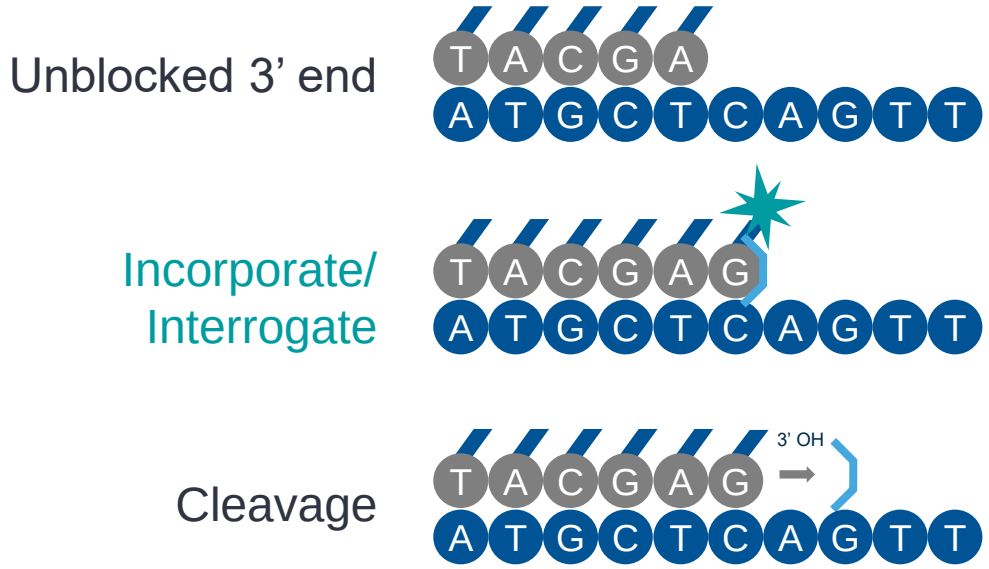
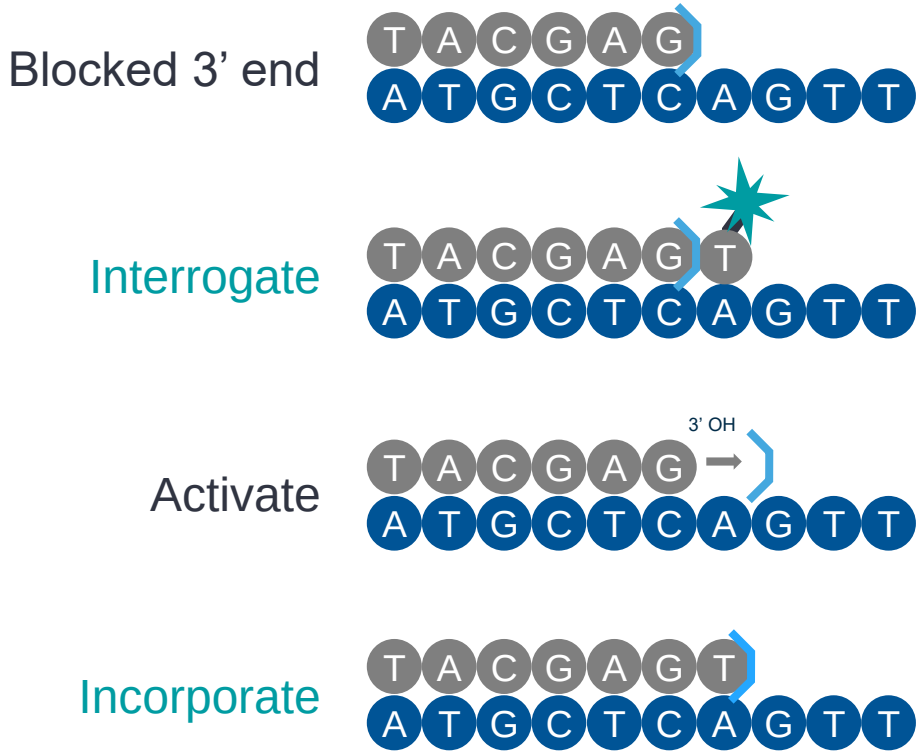
SBB advantages: Incorporates native nucleotides, produces unmodified DNA

No base modifications, no molecular scarring

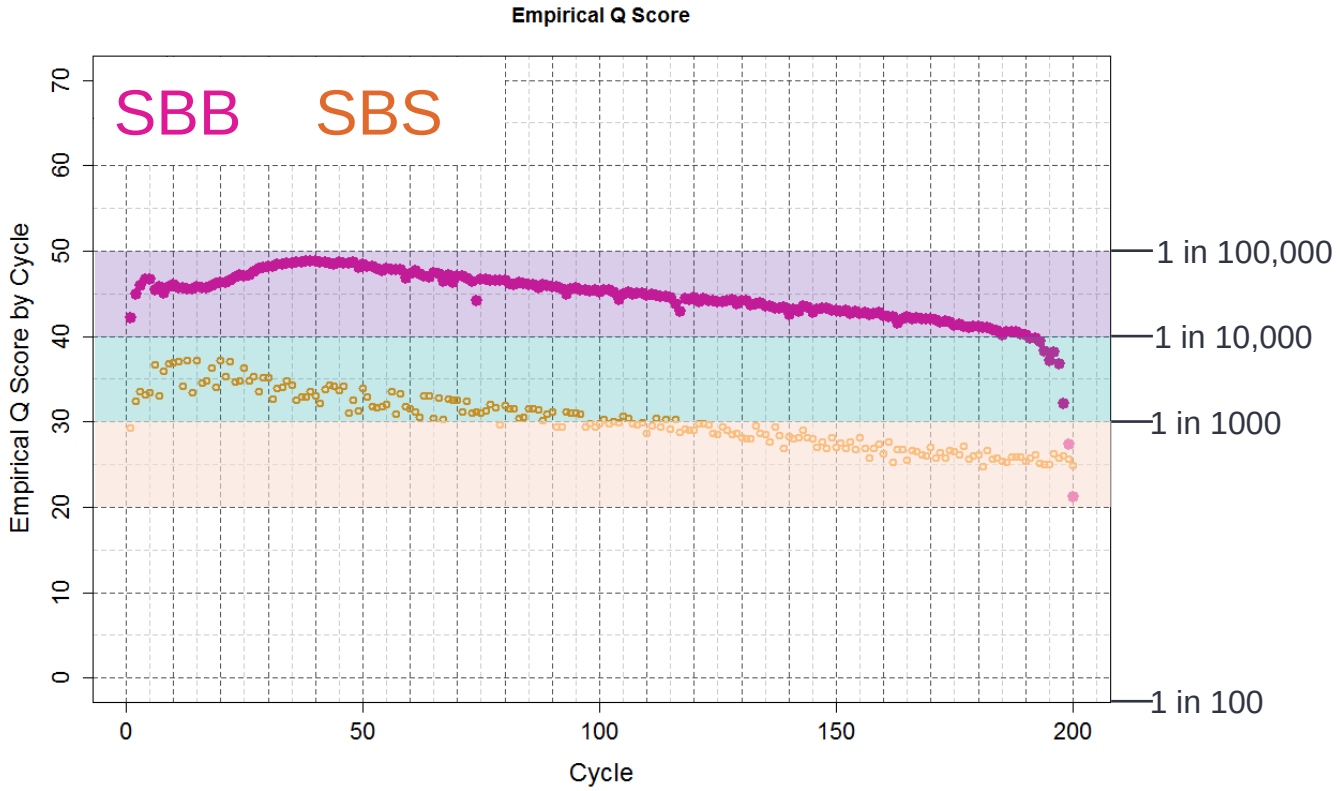
Sequencing by synthesis (SBS)



Sequencing by binding (SBB)



SBB accuracy - >90% of bases Q40+



SBB error rates ~15× lower at any given cycle, between 1:10,000 to 1:100,000

- Attain **near-perfect accuracy** in sequencing, changing standard parameters for multiple applications
- SBB error rates mean **not having to sequence at unnecessary depth**
- Reduces level of uncertainty
- Identify biological events that have critical implications

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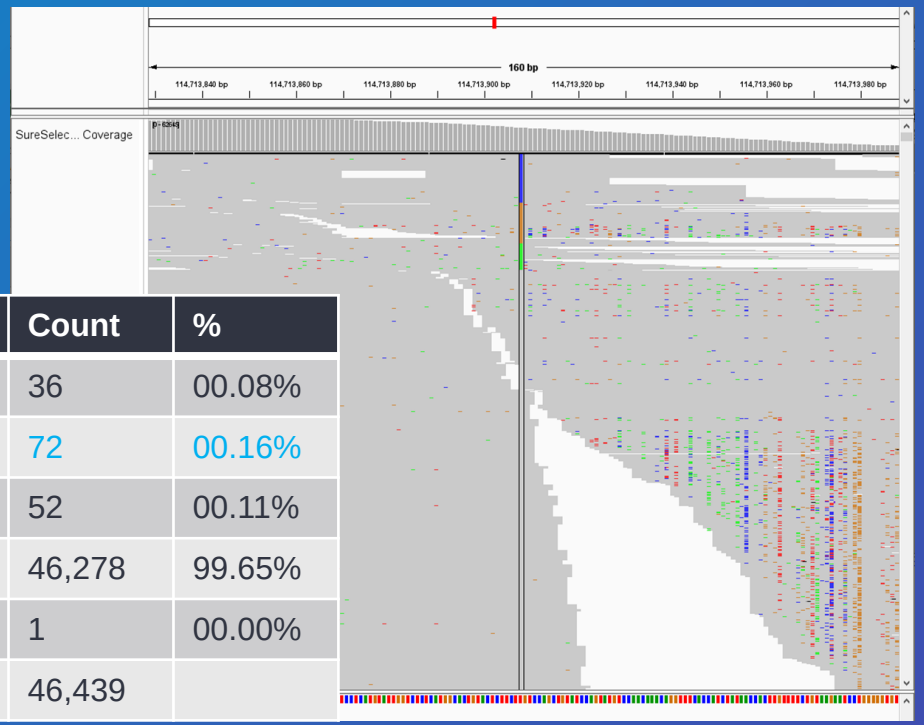
Chm13 sequencing. Empirical Q score evaluated on 99% of bases for each cycle.

Sequencing of true variant sample SBB vs SBS

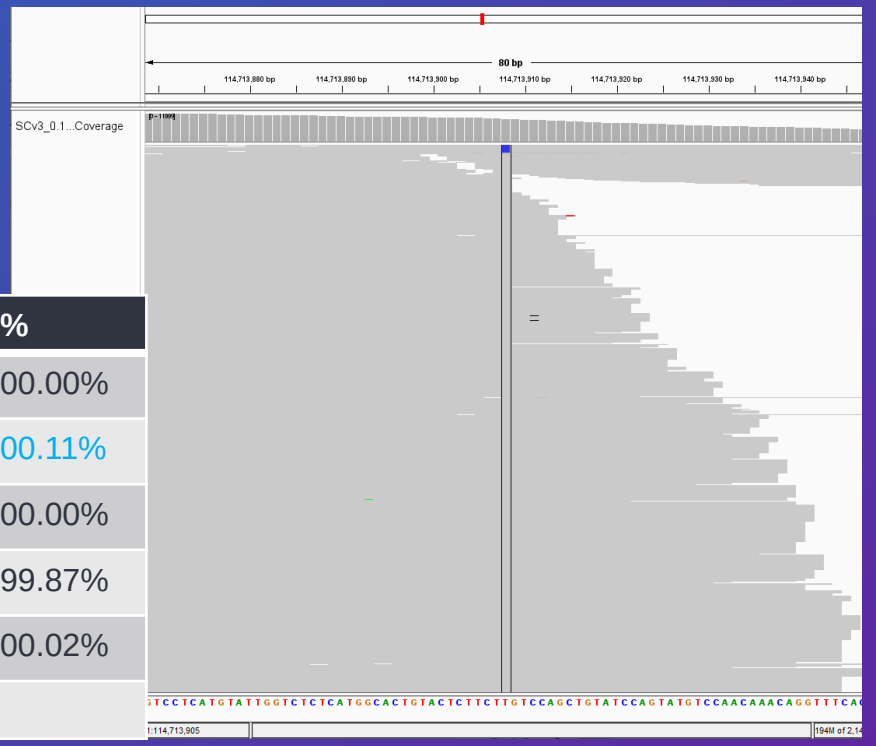
0.1% VAF NRAS Q61R

SBS 48,000x



Base	Count	%
A	36	00.08%
C	72	00.16%
G	52	00.11%
T	46,278	99.65%
N	1	00.00%
Total	46,439	

SBB 12,000x



Base	Count	%
A	0	00.00%
C	10	00.11%
G	0	00.00%
T	8,947	99.87%
N	2	00.02%
Total	8,959	

Revio™ system

1,300
WGS / Year

1- 4
SMRT Cells
in parallel

24 hr
Run time

50%
Fewer
consumables

>3x
Output per
SMRT Cell

$995 USD* / human genome (30x HiFi)

Onso™ system

400-500M
Reads

200 + 300
Cycle kits

48 hr
Run time

≥ 90%
Bases Q40+

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*U.S. list price is $995 for sequencing reagents for one Revio SMRT Cell, which has an expected yield of 90 Gb, equivalent to a 30X human genome. Your local sales representative can provide detailed pricing in your currency.