SCIENTIFIC POSTER

Mimix cfDNA reference material: mimicking human-like profiles.

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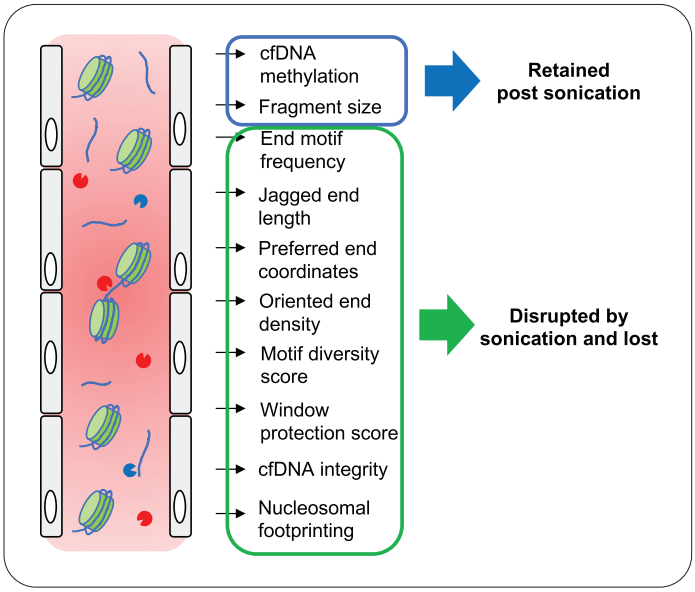
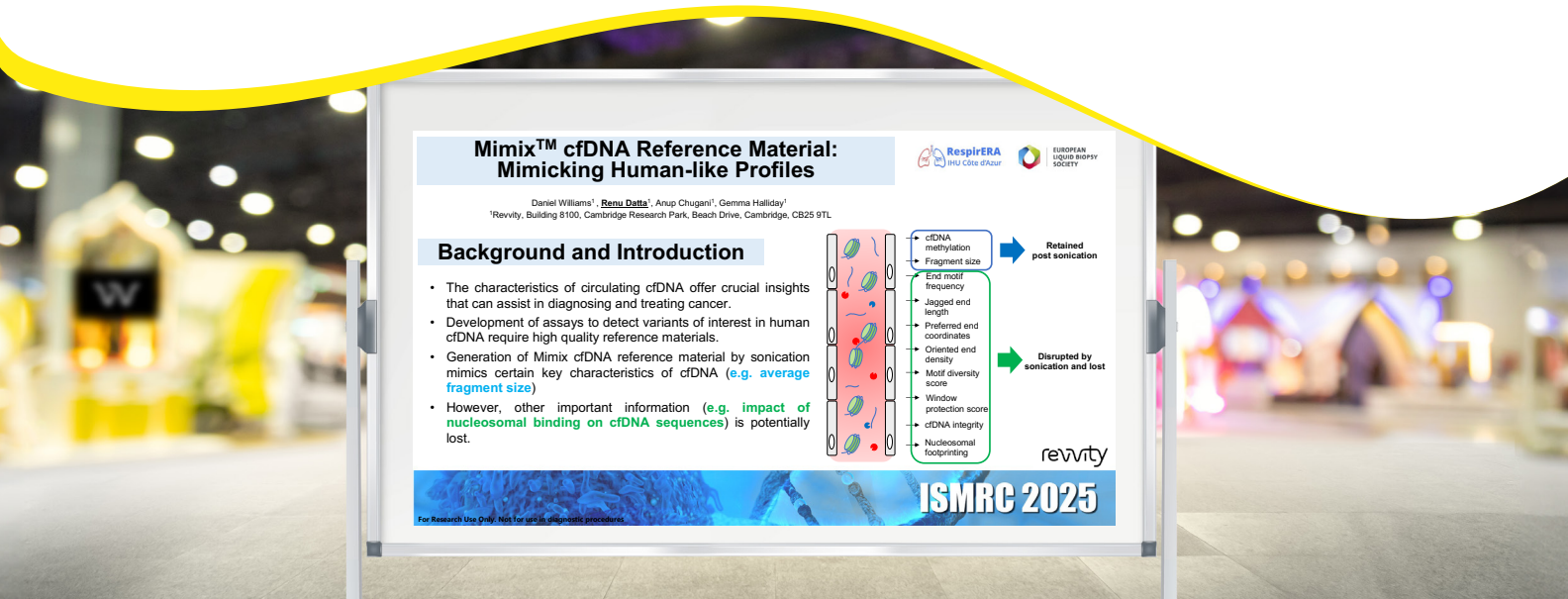
Background and Introduction

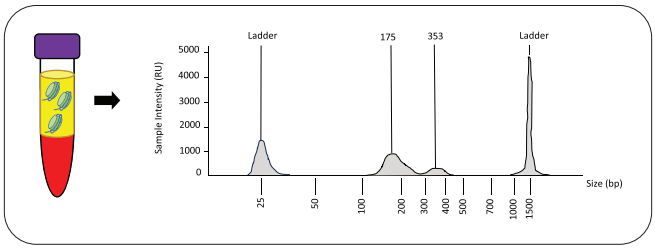
- The characteristics of circulating cfDNA offer crucial insights that can assist in diagnosing and treating cancer.
- Development of assays to detect variants of interest in human cfDNA require high quality reference materials.
- Generation of Mimix™ cfDNA reference material by sonication mimics certain key characteristics of cfDNA (e.g. average fragment size)
- However, other important information (e.g. impact of nucleosomal binding on cfDNA sequences) is potentially lost.





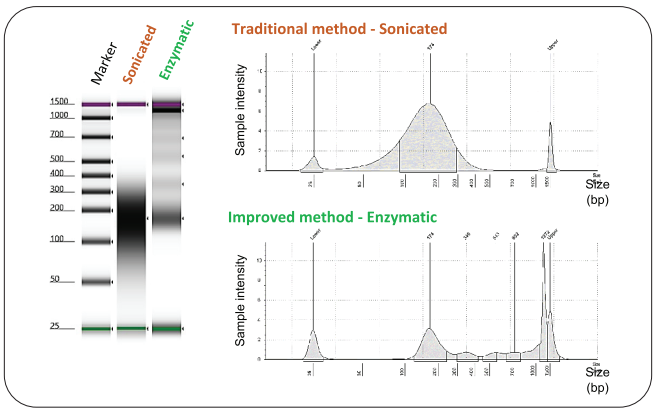
Results

Patient cfDNA profile



- cfDNA profiles isolated from human plasma show a prominent peak at 175bp alongside a smaller 353bp peak.
- Sonicated cfDNA reference material lacks this dual peak and shows a broader distribution of DNA fragments.
- Enzymatically fragmented cfDNA reference material more accurately mimics the size profile of cfDNA found in human plasma.
- Allelic frequencies measured by ddPCR are maintained after enzymatic fragmentation.

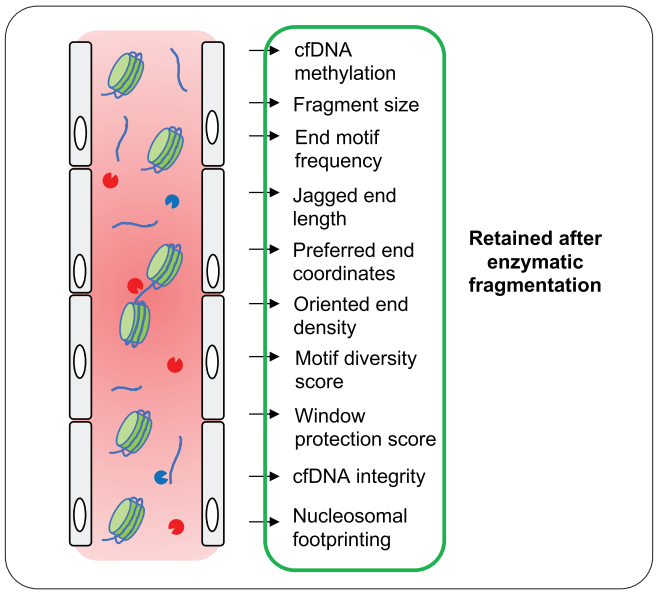
Mimix reference material profiles



Expected variant AF	Gene	Variant	AF post enzymatic (ddPCR)
50%	B-Raf	V600K	48.70%

Conclusion

- Generating cfDNA reference standards via enzymatic fragmentation represents a major improvement over sonicated cfDNA.
- Enzymatically fragmented cfDNA reference material more accurately represents patient ctDNA, capturing crucial details like fragmentation patterns and methylation.
- Revvity's team are currently in the process of characterising the features retained following enzymatic fragmentation that may be of use for the next generation of cfDNA based assays to support cancer diagnosis and treatment.



References

- Lo Y.M.D., Han D.S.C., Jiang P., Chiu R.W.K. Epigenetics, fragmentomics, and topology of cell-free DNA in liquid biopsies. Science. 2021;372:eaaw3616. doi: 10.1126/science.aaw3616.
- Snyder M.W., Kircher M., Hill A.J., Daza R.M., Shendure J. Cell-free DNA comprises an *in vivo* nucleosome footprint that informs its tissues-of-origin. Cell. 2016;164:57-68. doi: 10.1016/j.cell.2015.11.050.