BIOCAPTIVA

DNA CAPTURE FOR LIQUID BIOPSY

UNLOCK THE FULL POTENTIAL OF cfDNA

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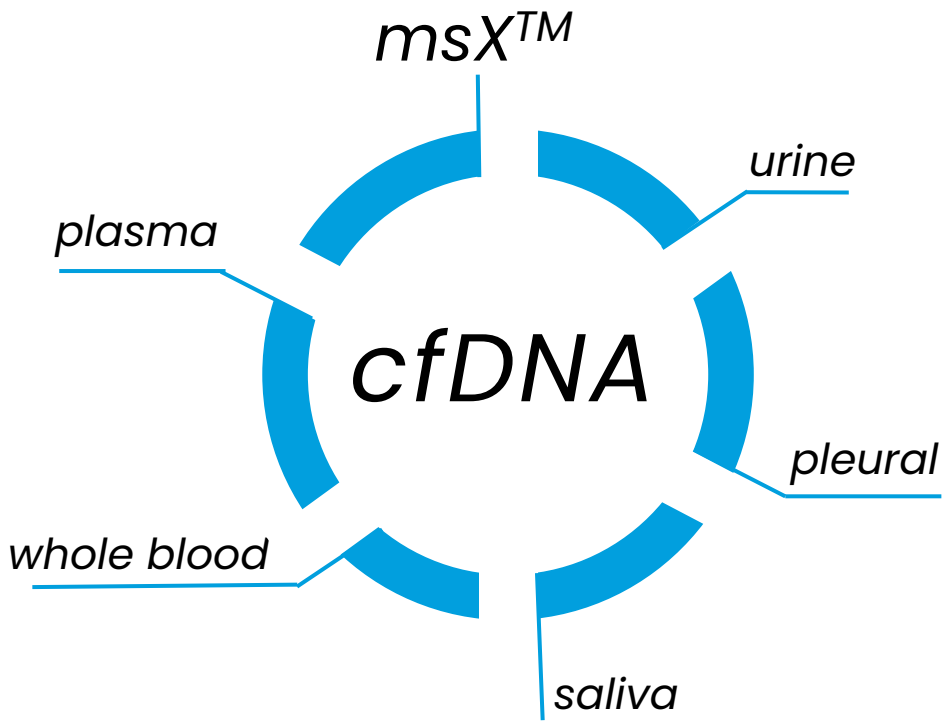
msX™ – platform technology for cfDNA capture

- msX™ is a range of polymers that extract cfDNA directly from biological and non-biological fluids
- A ubiquitous platform able to coat any liquid accessible substrate
- Native cfDNA binding with application dependent sample volumes without biofouling
- Zero additives required, sample integrity is preserved, ideal for multi-omic applications
- Simple, scalable processing workflows



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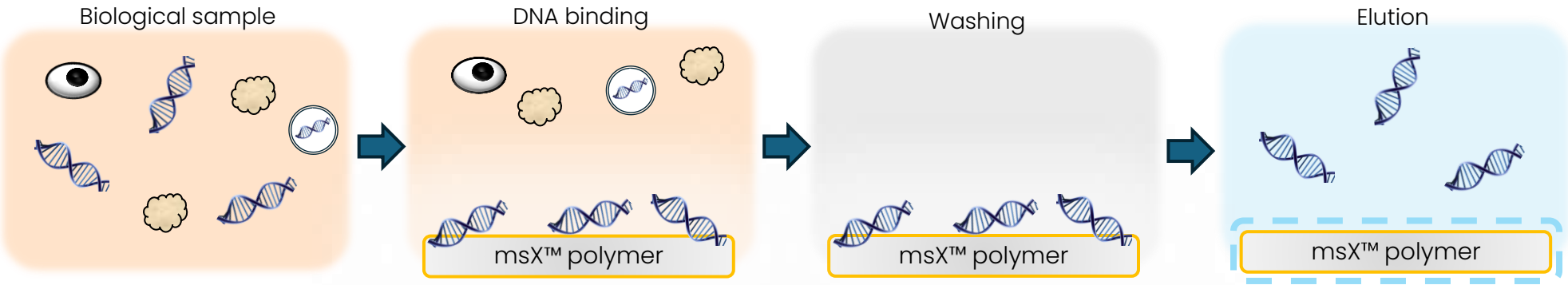
Polymer mechanism



cfDNA is found in a complex mixture of other biomolecules, cells and vesicles

msX™ polymer selectively binds the truly cell-free DNA without the addition of any reagents

Once bound, other components are washed away

DNA is released back into solution to provide a highly enriched cfDNA sample

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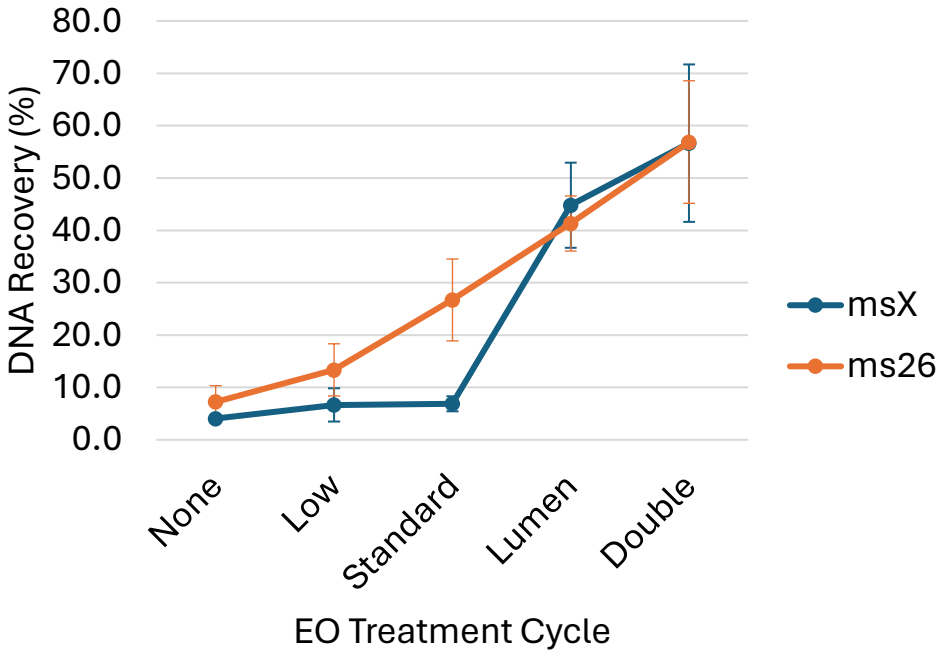
Ethylene oxide impact

- EO retains functionality and enhances DNA capture efficiency of msX™ polymer-coated materials
- Strong EO treatment of msX™ polymers produce a 5-fold increase in cfDNA recovery from plasma
- **The use of EO-treated msX™ polymers can be used to improve DNA recovery from biofluids**



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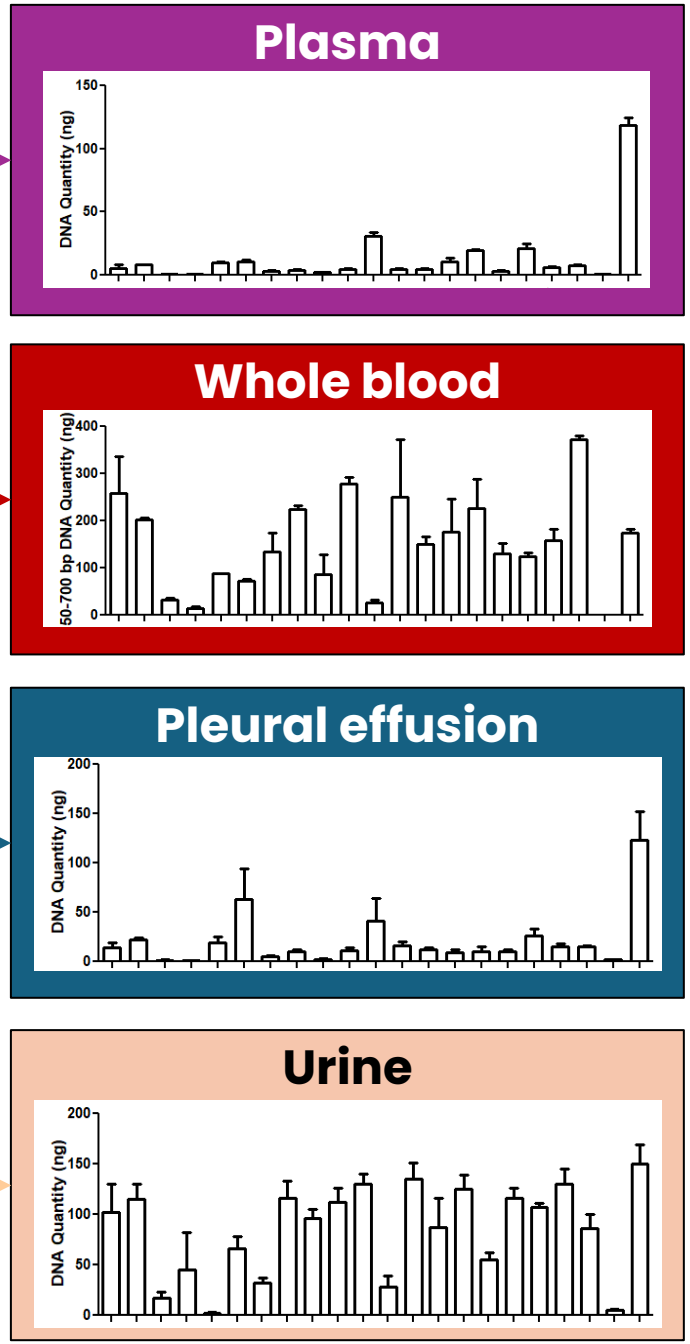
Ex vivo applications

- msX™ polymers were optimized for in vivo cfDNA recovery from plasma.
- Versions of these polymers are suitable for other biofluid applications
- The varying composition of these biofluids and clinical considerations around their analysis require bespoke polymers
- A polymer library (20 polymers) was created and tested with plasma, whole blood, pleural effusion, and urine
- Lead candidates with effective cfDNA binding have been identified for each biofluid, and are currently being scaled up
- msX™ polymers can be tailored for use in various complex biofluids

Polymer library



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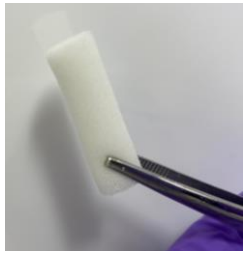
Example - msX™ polymer vs QIAamp

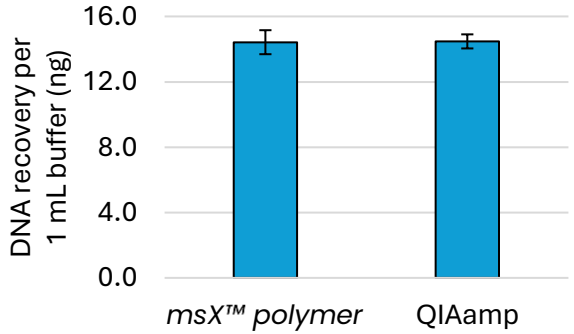
DNA recovery from **buffer**

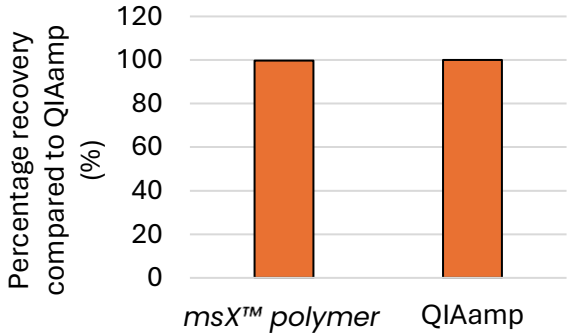
- msX™ polymers can recover DNA from buffer with the same efficiency as the QIAamp extraction kit

Input	Extraction method	Input volume (mL)	Purified volume (mL)	Total DNA recovery (ng)	DNA recovery per 1 mL input (ng)	Percentage recovery per 1 mL compared to QIAamp (%)
DNA-spiked buffer	*msX™ polymer*	*10*	*0.1*	*144*	*14.4*	*99.6*
	QIAamp kit	*2 x 5*	*2 x 0.05*	*145*	*14.5*	*100*



msX™ polymer-coated sponge cylinders (2.5 cm^3, non-EO)





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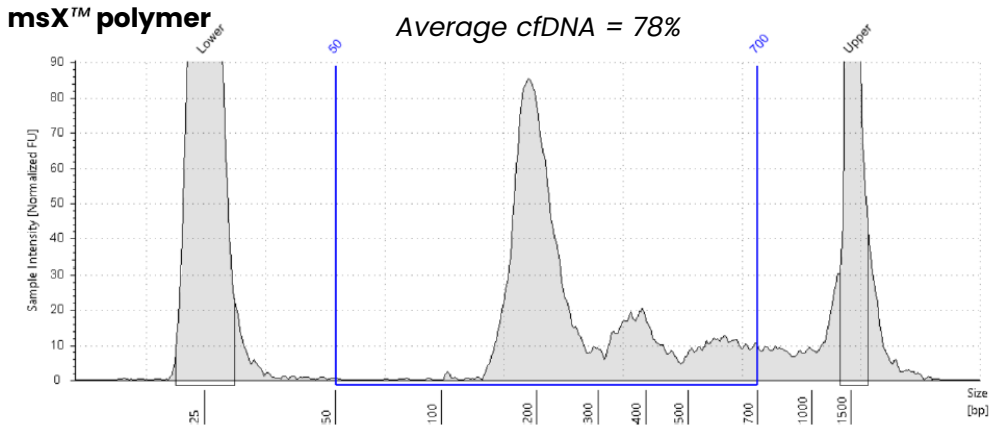
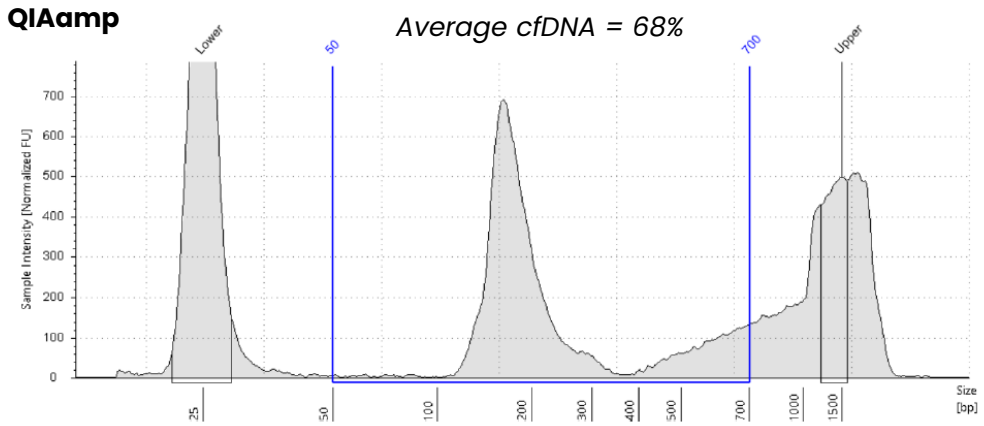
Example - msX™ polymer vs QIAamp

DNA recovery from **plasma**

- DNA recovered by msX™ polymers are enriched for lower molecular weight fragments compared to the QIAamp (78% vs 68%)
- The QIAamp introduces substantial high molecular weight DNA that is not present with the msX™ polymers





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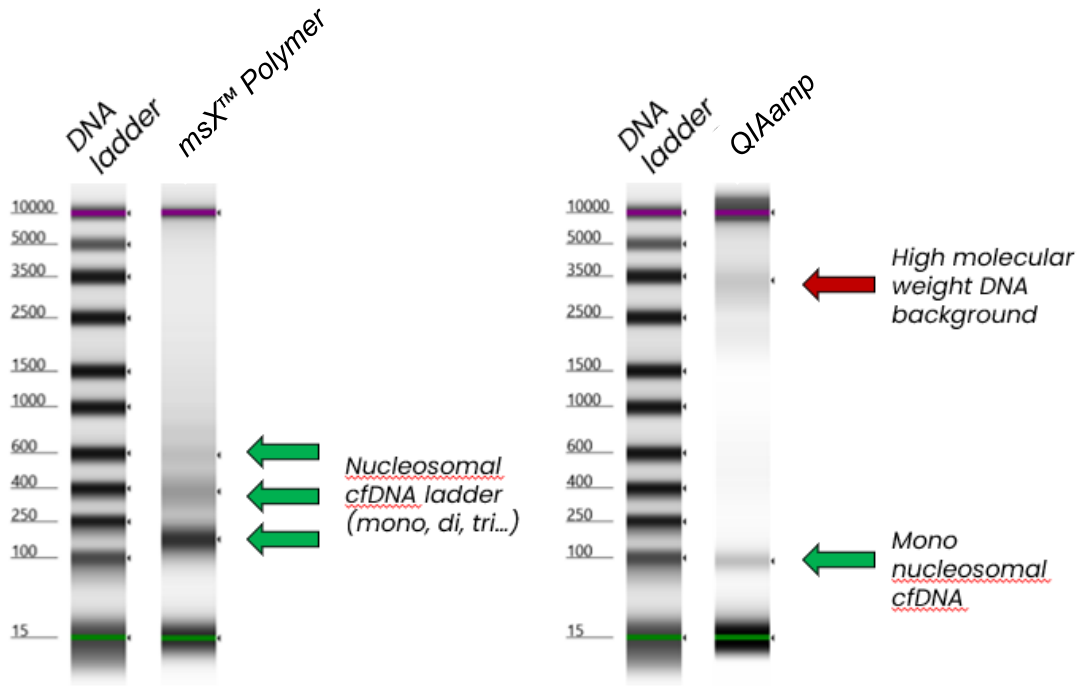
Example - msX™ polymer vs QIAamp

Improved **signal-to-noise ratio**

- *msX™ polymers specifically enrich for cfDNA while maintaining sample integrity*
- *Extraction of cfDNA through destructive processes (QIAamp) introduces contaminating sources of high molecular weight DNA*
- *cfDNA samples recovered by msX™ polymers have improved signal-to-noise ratio*
- **Combined with an unlimited sample size, msX™ polymers provide both higher quantity and quality cfDNA samples, increasing the performance of downstream assays**



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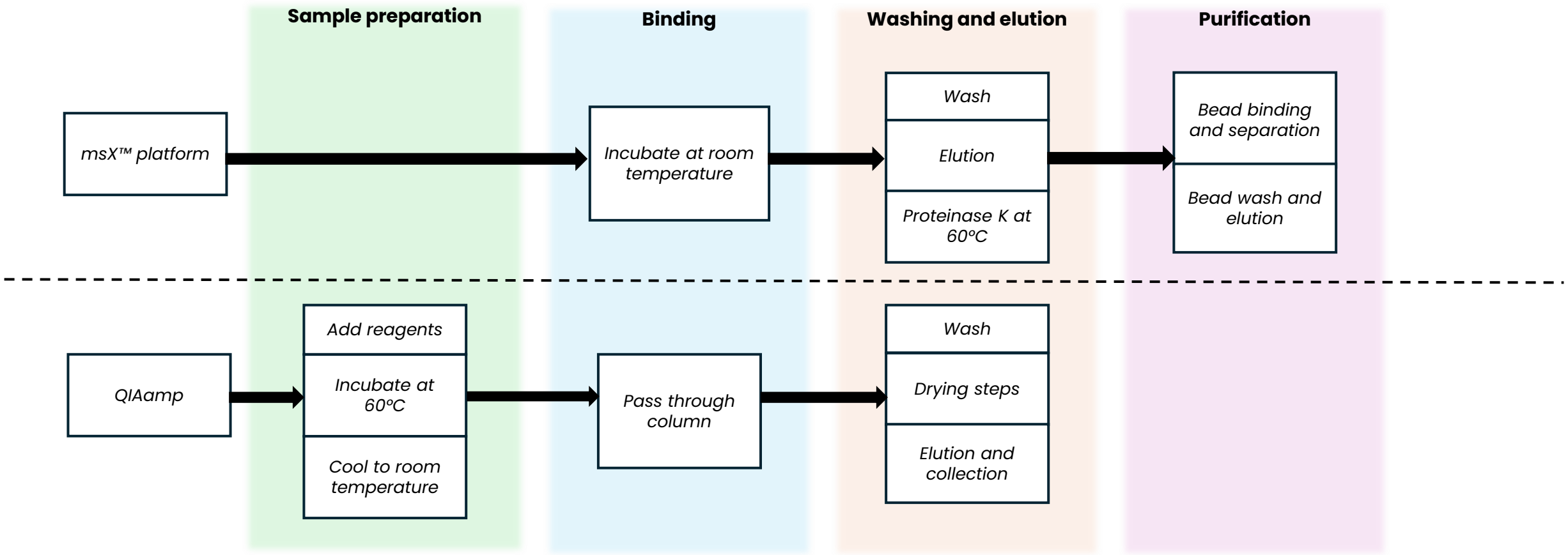
msX™ vs QIAamp: Process Flow



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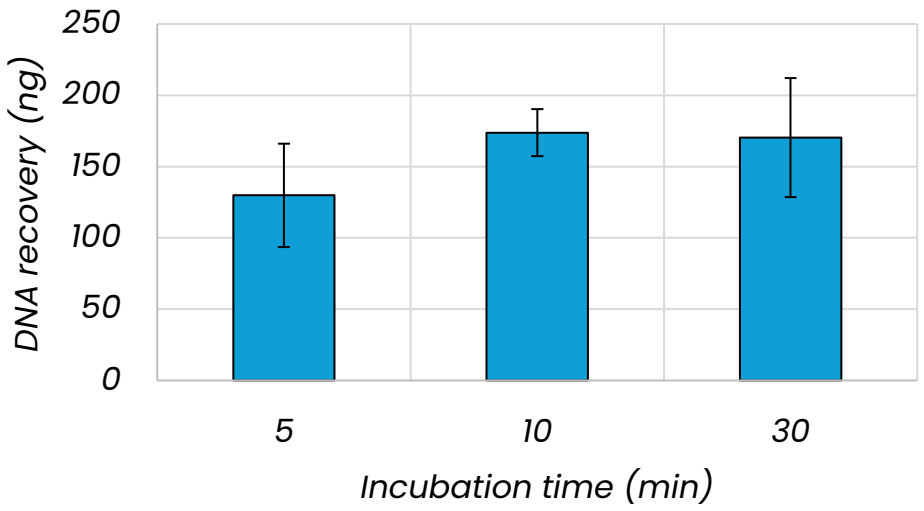
Plasma DNA binding time course

- cfDNA is quickly bound to the msX™ polymer surface providing flexibility over how the coated substrates are used e.g. static and flow applications
- Maximum DNA binding of cfDNA from plasma is achieved within 10 min



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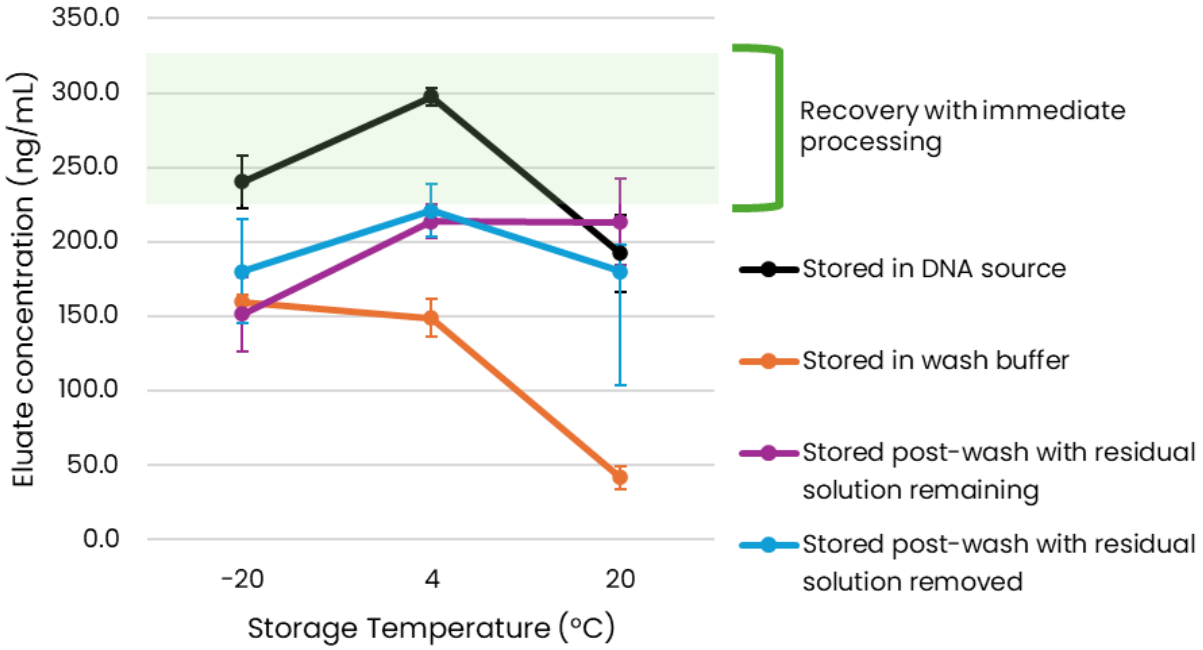
DNA stabilization and on-polymer storage for 1 month

- DNA can be stored on the polymer substrate without loss in recovery upon eventual elution
- Conditions have been investigated for the storage of polymer-bound DNA for 1 month
- Storage with high recovery was possible across the temperatures explored, including room temperature
- **msX™ polymers can be used to both collect and stabilize/store cfDNA for >1 month**



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msX™ Polymers Overview

	msX™ polymer	QIAamp
Input volume	*Unlimited*	*1-5 mL*
Estimated recovery	*Tested up to 5000 ng*	*5-50 ng*
Method of increasing DNA recovery	*Promoting further interaction with the polymer:* • *Increasing input volume* • *Increasing incubation* • *Increasing device size* • *Changing flow rate*	*Pooling multiple extracts*
Additives	*None*	*Toxic lysis and binding reagents:* • *Proteases* • *Guanidinium compounds* • *Surfactants*
Possible contaminants	*Minimal*	• *Cellular DNA* • *Encapsulated DNA* • *Complexed DNA*
Signal-to-noise	*Enriched for cfDNA*	*Reduced by contaminants*
Biofluids	*All*	*Plasma, serum, urine*

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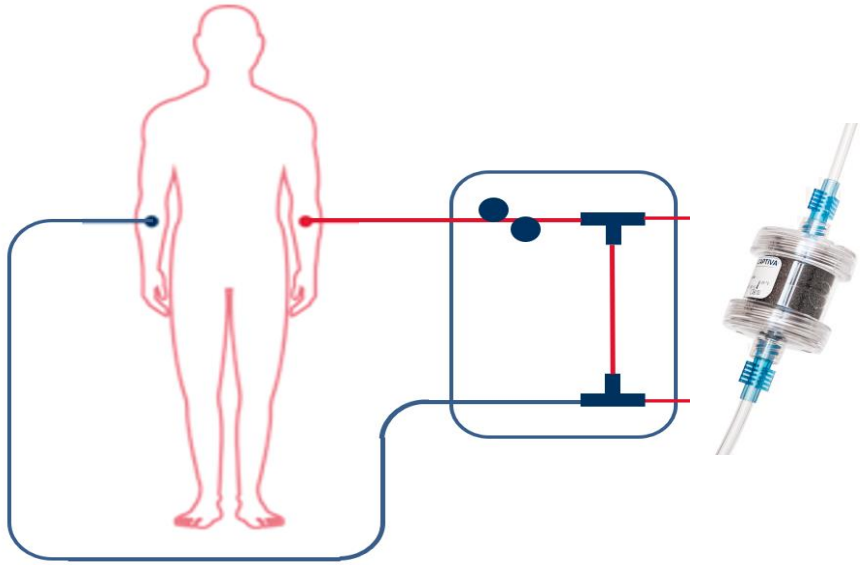
Medical device in-vivo application: BioCaptis

First in class apheresis column for cfDNA capture

- Single-use OEM device containing msX™-coated substrate
- Device used during standard plasma-separating apheresis procedure (30-40 mins)
- Functional prototypes demonstrated recovery of up to 100-fold increase in cfDNA compared to 10 mL blood draw
- FIH trials to begin H1 2024



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Partnership Opportunities

Research

Collaboration with new / supporting data for uses of cfDNA from biological fluids. Wide range of possible applications (*in vivo* and *ex vivo*).

BioCaptiva will offer optional lab processing (elution, concentration, cfDNA size & quality).

Clinical Trials

Use of cfDNA as a captured metric / source of input data to support clinical trials. FDA anecdotally enthusiastic for this capability. Wide range of applications.

Opportunity to become the gold-standard for monitoring progress of oncology trials and treatment effectiveness.

Diagnostics

Use of cfDNA in a standalone diagnostic or in a companion diagnostic for any oncology treatment. The decision maker and customer shall be the diagnostic company.

For use in any molecular diagnostic assay requires quality / quantity of cfDNA.

Ex vivo

POLYMER ONLY

Use of polymer in development of medical device or diagnostics in *ex vivo* applications that can benefit / require larger sample volumes / multi-omic uses and product development.

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