Ambient Temperature Preservation of Human FFPE Tumor-Derived Nucleic Acids with Encapsulation Technology

Lee Organick[1], Michael Blas[1], Benjamin Haibe-Kains[2], James Banal[1], Celeste Yu[2], Farnoosh Abbas-Aghababazadeh[2], Philippe L. Bedard[2]

1. Cache DNA, San Carlos USA
2. University Health Network, Princess Margaret Cancer Research Centre, Toronto Canada

Conflict of Interest Disclosure

The following authors are employees of Cache DNA and hold stock:

- Lee Organick
- Michael Blas
- James Banal

Lee

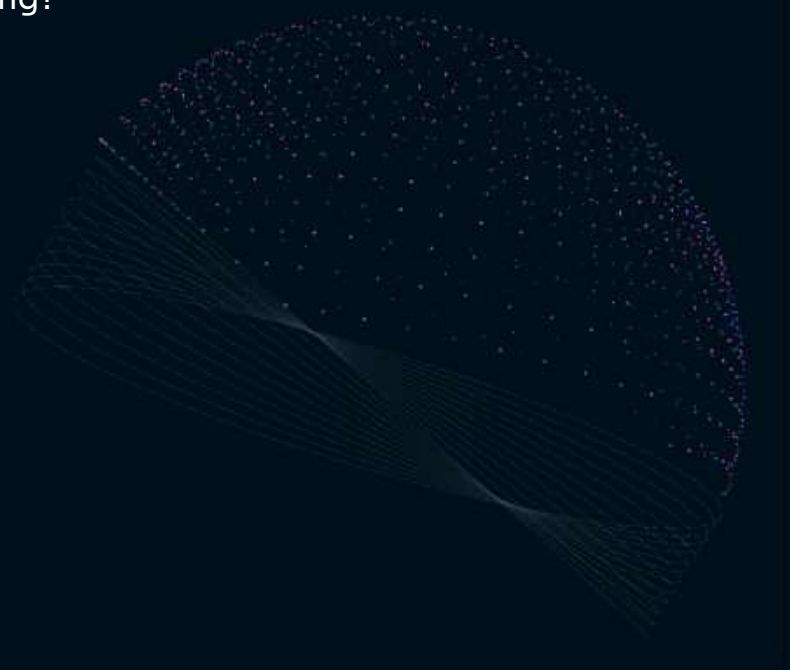
The following authors have **no conflicts of interest** to declare:

- Benjamin Haibe-Kains
- Celeste Yu
- Farnoosh Abbas-Aghababazadeh
- Philippe L. Bedard

Farnoosh

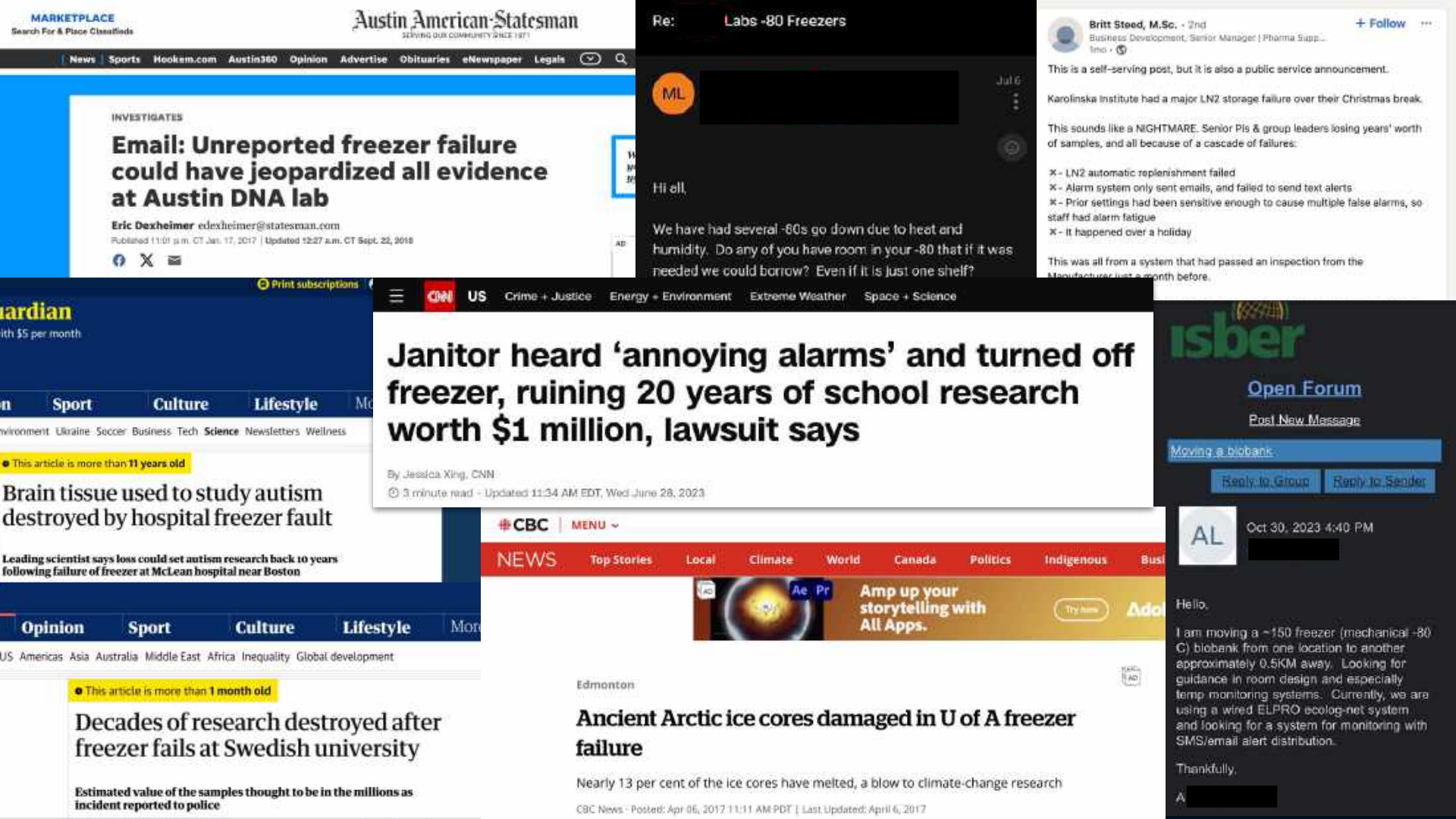
Agenda: Ambient Temperature Preservation of Nucleic Acids

- What technical challenges are biobanks currently facing?
- Introduction to Caching
- Collaboration with UHN and Cache
- Questions



What technical challenges are biobanks currently facing?

1. Freezer logistics
    - Maintenance
    - Monitoring and responses
    - Redundant aliquots to prevent freeze-thaws
    - Emergencies and accidents


MARKETPLACE
Search For & Place Classifieds
Austin American-Statesman
SERVING OUR COMMUNITY SINCE 1871
News | Sports | Hookem.com | Austin360 | Opinion | Advertise | Obituaries | eNewspaper | Legals
INVESTIGATES
Email: Unreported freezer failure could have jeopardized all evidence at Austin DNA lab
Eric Dexheimer edexheimer@statesman.com
Published 11:01 p.m. CT Jan. 17, 2017 | Updated 12:27 a.m. CT Sept. 22, 2018
Re: Labs -80 Freezers
ML
Jul 6
Hi all,
We have had several -80s go down due to heat and humidity. Do any of you have room in your -80 that if it was needed we could borrow? Even if it is just one shelf?
Britt Steed, M.Sc. · 2nd
Business Development, Senior Manager | Pharma Supp...
1mo ·
+ Follow
This is a self-serving post, but it is also a public service announcement.
Karolinska Institute had a major LN2 storage failure over their Christmas break.
This sounds like a NIGHTMARE. Senior PIs & group leaders losing years' worth of samples, and all because of a cascade of failures:
✕ - LN2 automatic replenishment failed
✕ - Alarm system only sent emails, and failed to send text alerts
✕ - Prior settings had been sensitive enough to cause multiple false alarms, so staff had alarm fatigue
✕ - It happened over a holiday
This was all from a system that had passed an inspection from the
Print subscriptions
uardian
ith $5 per month
n Sport Culture Lifestyle
vironment Ukraine Soccer Business Tech Science Newsletters Wellness
This article is more than 11 years old
Brain tissue used to study autism destroyed by hospital freezer fault
Leading scientist says loss could set autism research back 10 years following failure of freezer at McLean hospital near Boston
CNN US Crime + Justice Energy + Environment Extreme Weather Space + Science
Janitor heard 'annoying alarms' and turned off freezer, ruining 20 years of school research worth $1 million, lawsuit says
By Jessica Xing, CNN
3 minute read · Updated 11:34 AM EDT, Wed June 28, 2023
isber
Open Forum
Post New Message
Moving a biobank
Reply to Group
Reply to Sender
AL
Oct 30, 2023 4:40 PM
Hello,
I am moving a ~150 freezer (mechanical -80 C) biobank from one location to another approximately 0.5KM away. Looking for guidance in room design and especially temp monitoring systems. Currently, we are using a wired ELPRO ecolog-net system and looking for a system for monitoring with SMS/email alert distribution.
Thankfully,
Opinion Sport Culture Lifestyle
US Americas Asia Australia Middle East Africa Inequality Global development
This article is more than 1 month old
Decades of research destroyed after freezer fails at Swedish university
Estimated value of the samples thought to be in the millions as incident reported to police
CBC MENU
NEWS Top Stories Local Climate World Canada Politics Indigenous
Amp up your storytelling with All Apps.
Edmonton
Ancient Arctic ice cores damaged in U of A freezer failure
Nearly 13 per cent of the ice cores have melted, a blow to climate-change research
CBC News · Posted: Apr 06, 2017 11:11 AM PDT | Last Updated: April 6, 2017

What technical challenges are biobanks currently facing?

1. Freezer logistics
    - Maintenance
    - Monitoring and responses
    - Emergencies and accidents
    - Redundant aliquots to prevent freeze-thaws
2. Running out of space or electrical capacity
3. Nucleic acids degrade over time
    - Main causes of degradation are water and air[1]
    - DNA in FFPE degrades 2x faster than extracted DNA[2]

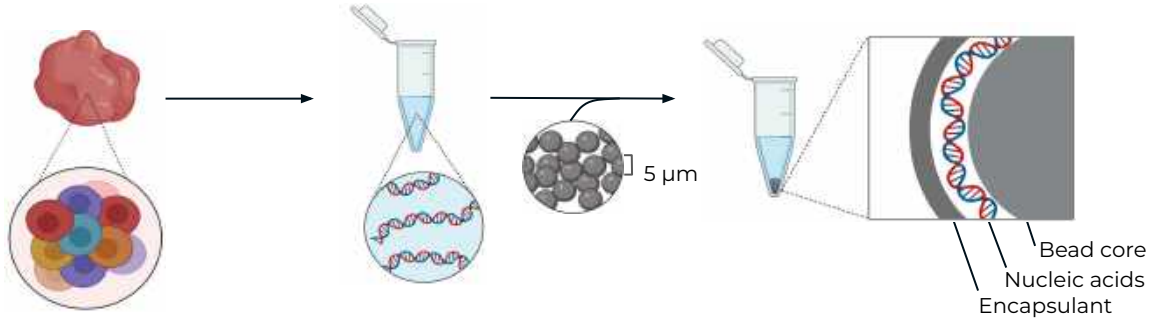
1. Colotte *et al.* Adverse Effect of Air Exposure on the Stability of DNA Stored at Room Temperature. *Biopreservation and Biobanking,* https://doi.org/10.1089/bio.2010.0028
2. Guyard *et al.* DNA degrades during storage in formalin-fixed and paraffin-embedded tissue blocks. *Virchows Arch* 471, 491–500 (2017). https://doi.org/10.1007/s00428-017-2213-0

What's wrong with alternative ambient temperature nucleic acid preservation methods?

There are very few storage solutions available. Most are not scalable (to store or retrieve), too expensive, or do not offer adequate protection.

	Additives	Lyophilization	Micro-scale encapsulation	Macro-scale encapsulation
Storage Method	Mix in additive Optional: dehydrate	Complex configurations Specialized equipment Large footprint	Multi-step process Standard lab equipment Benchtop footprint	Samples must be shipped to encapsulator
Recovery Method	Rehydration (1-10 minutes)	Rehydration (1-10 minutes)	De-encapsulation (10-15 minutes)	De-encapsulation (5-10 minutes)
Can Take Aliquots	No	No	Yes	No
Slows Degradation	Only in low-humidity conditions	Yes Likely 10s-100s of years	Yes 10s-100s of years	Yes 1000s of years
Scalable	No	Maybe	Yes	No

Caching nucleic acids



1. **Nucleic acids are extracted**
2. **Beads and encapsulant are introduced**
3. **Nucleic acids are encapsulated**

Peer-reviewed publications on proof-of-concept

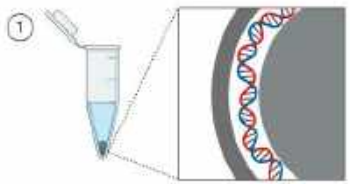
10.1021/acsami.1c14985
10.1038/s41563-021-01021-3

Storage of genomes & RNA
Random access retrieval

Intellectual Property

Growing patent portfolio supporting core platform technology
Cache DNA, Inc. has rights to the methods described herein

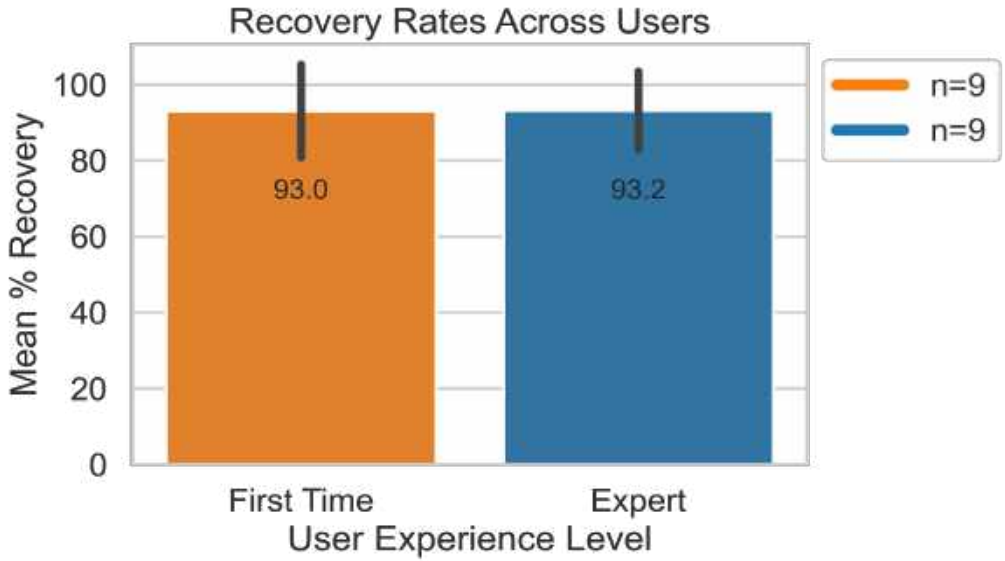
Recovery Rate



Aliquot, De-encapsulate

Quantify

Qubit



Note: *Recent Caching of FFPE-derived DNA shows mean recovery rate of 93%.*

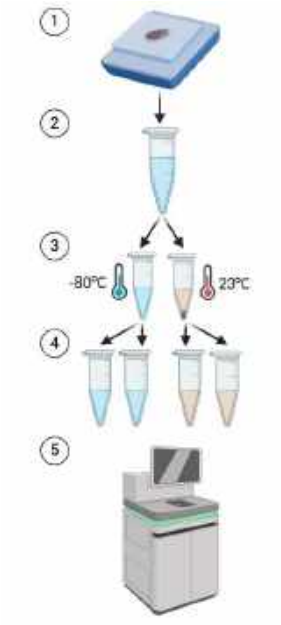
Partnering with University Health Network, Princess Margaret Cancer Research Centre (PM)

Cache is committed to preserving nucleic acids **without compromising quality.** We understand these **samples are precious,** vital for **patient well-being,** and key to **enabling research** to help future patients.

We have partnered with PM to:

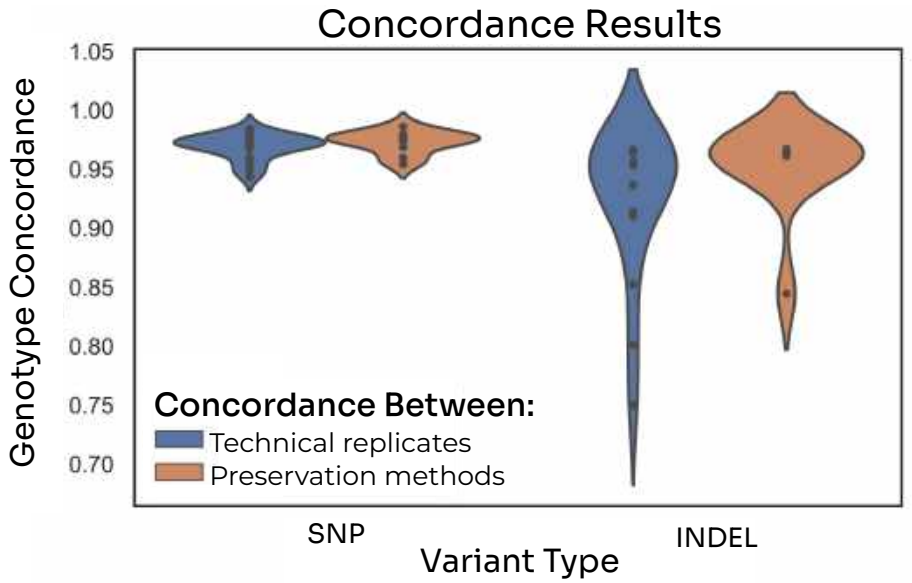
1. **Encapsulate a greater diversity** of nucleic acid origins
2. Perform a **rigorous evaluation of sequence-level changes**

Aim 1 Experimental Overview



1. 10 formalin fixed paraffin embedded (FFPE) tumor samples
2. DNA was extracted and shipped to Cache.
3. Half of each sample was kept frozen, half was Cached.
4. After 1 month, samples were retrieved and split as technical replicates.
5. All 40 samples were prepared for whole genome sequencing (WGS) and sequenced with a NovaSeq.

Result: Sequence Concordance Established



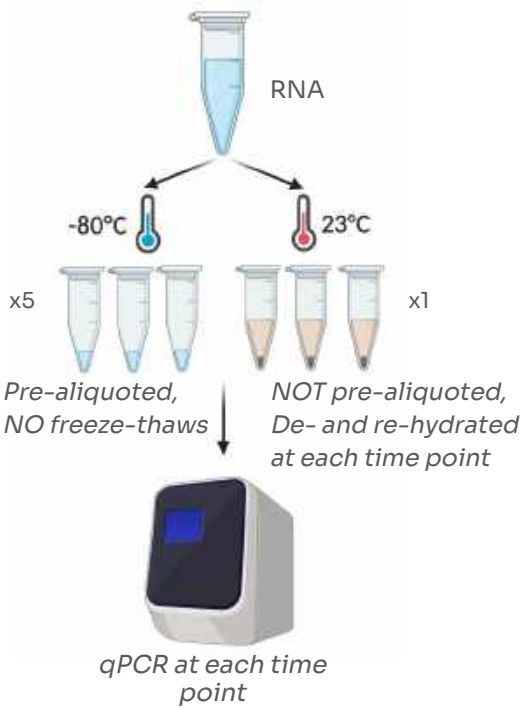
Please Note:

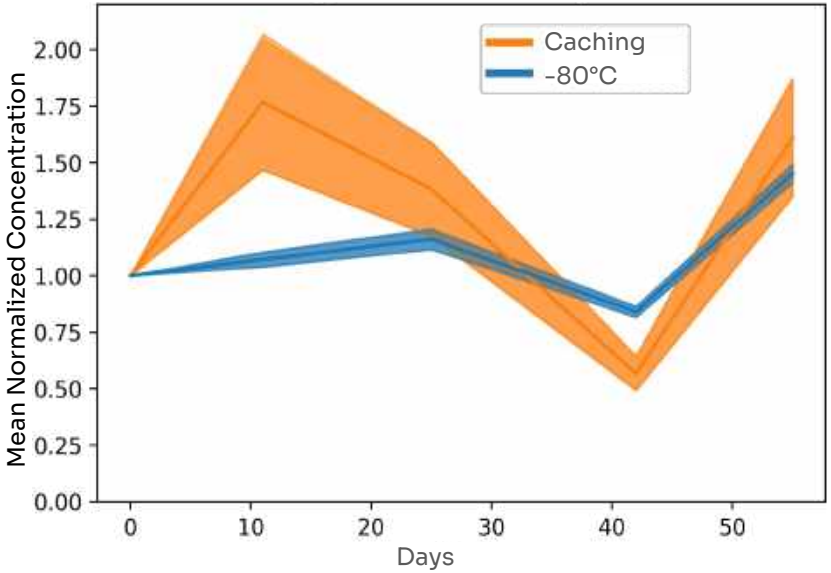
- Caching does not alter DNA sequences.
- We show whole genome sequence concordance between -80°C and Caching.

The Mutect2 variant caller was used on each sample to evaluate:

- Technical replicate concordance
- Preservation method concordance

Preliminary Data Motivating Aim 2 (RNA)



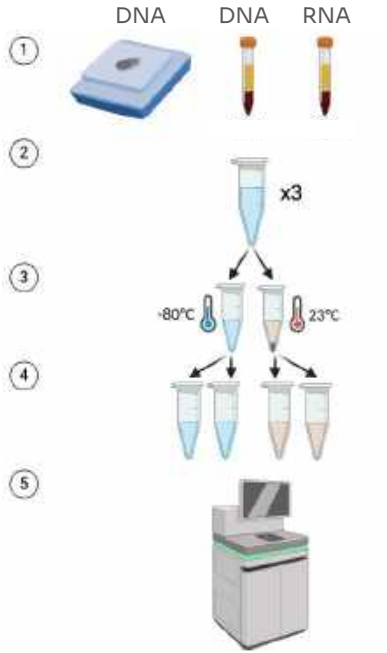


Caching successfully preserves RNA with no measurable degradation after 2 months.

Successful Completion Leads to Aim 2:

1. Caching is a **modular** part of UHN's typical pipeline
    - Utilizing the UHN whole genome and transcriptome sequencing **(WGTS) pipeline**
    - Evaluate **concordance**
2. Caching at **scale**
3. Caching of **RNA** clinical samples

Aim 2 Experimental Overview



1. 19 patients identified. Two DNA samples (paired tumor-normal), one RNA sample per patient.
2. DNA/RNA extracted and shipped to Cache.
3. Half of each sample kept frozen, half Cached.
4. After 1 month, samples retrieved and split in two for technical replicates.
5. All 57 (19 x 3) samples and their replicates (a total of 114 samples) shipped to UHN lab and run through their WGTS pipeline.

Summary

1. Cache preserves DNA and RNA at room temperature for long periods of time and does not compromise on quality
2. Cache is working with UHN to determine sequence concordance for DNA and RNA
    - We have found whole genome sequencing concordance between -80°C and Caching
3. Unless **you** act, current problems with nucleic acid preservation will persist. We want to live in a world with no freezers. Join us!

1. Apply for your kit (1 min)
2. Receive your invitation
3. Schedule a consultation (30 min Zoom)
4. Receive your early access kit
5. Share your experience (45 min Zoom)

Acknowledgements

UHN Princess Margaret Cancer Centre

Farnoosh Abbas-Aghababazadeh

Benjamin Haibe-Kains

Celeste Yu

Philippe L. Bedard

Cache DNA

Lee Organick

Michael Blas

James Banal