



**BiomiLab**



— BUREAU OF —  
RECLAMATION

# Cell lines to advance mollusk biology and biocontrol of invasive mussels

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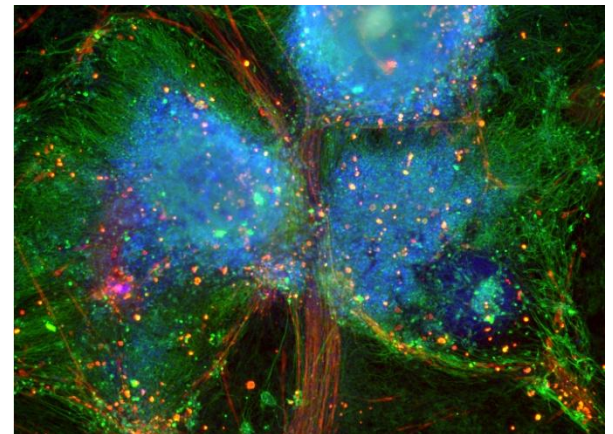
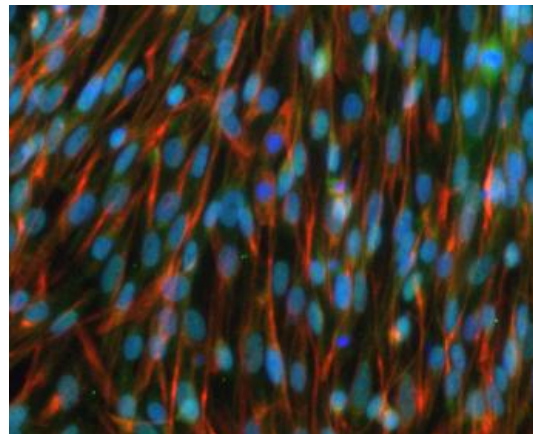
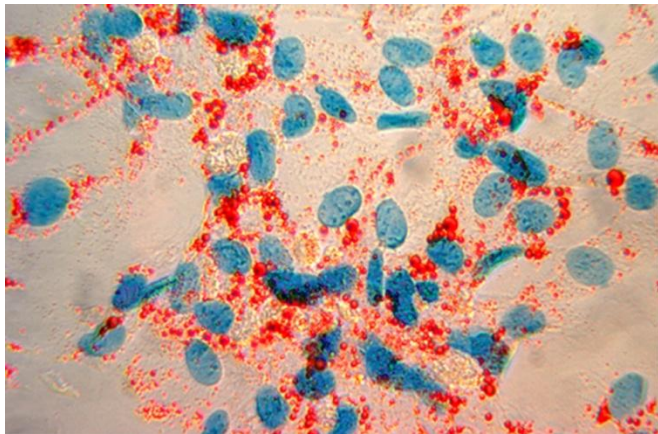
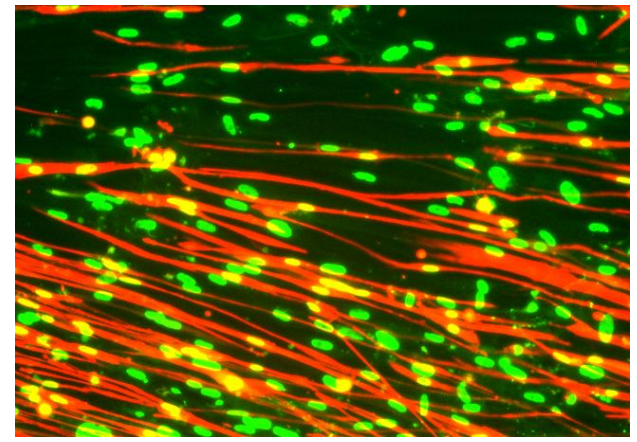
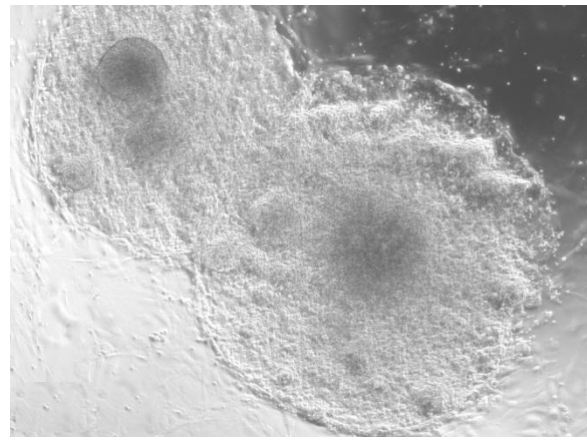
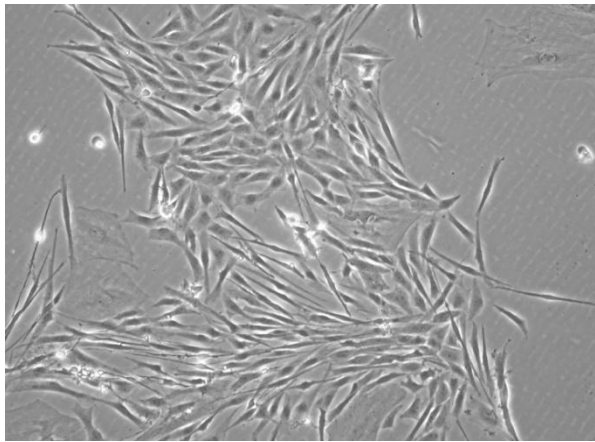
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Jacque Keele  
Yale Passamanek**

US Bureau of Reclamation  
Denver, CO

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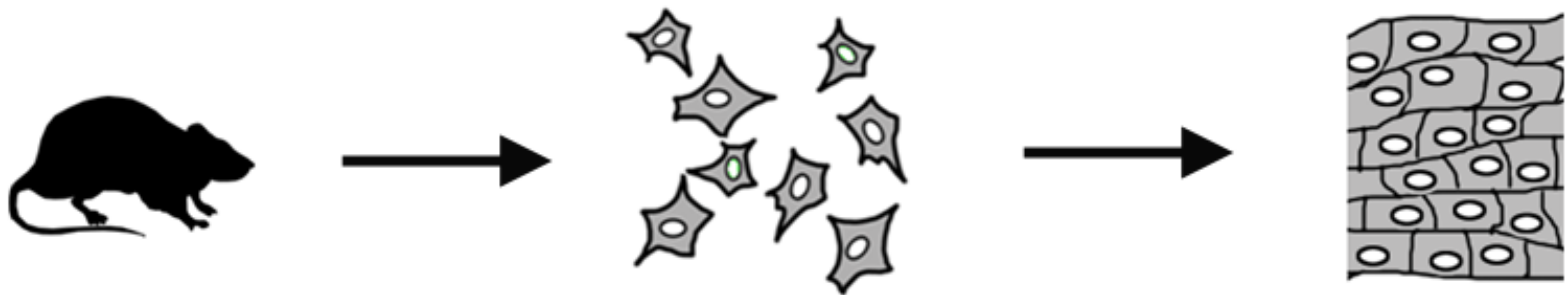


# Cultured cells are invaluable tools for understanding basic biology and disease



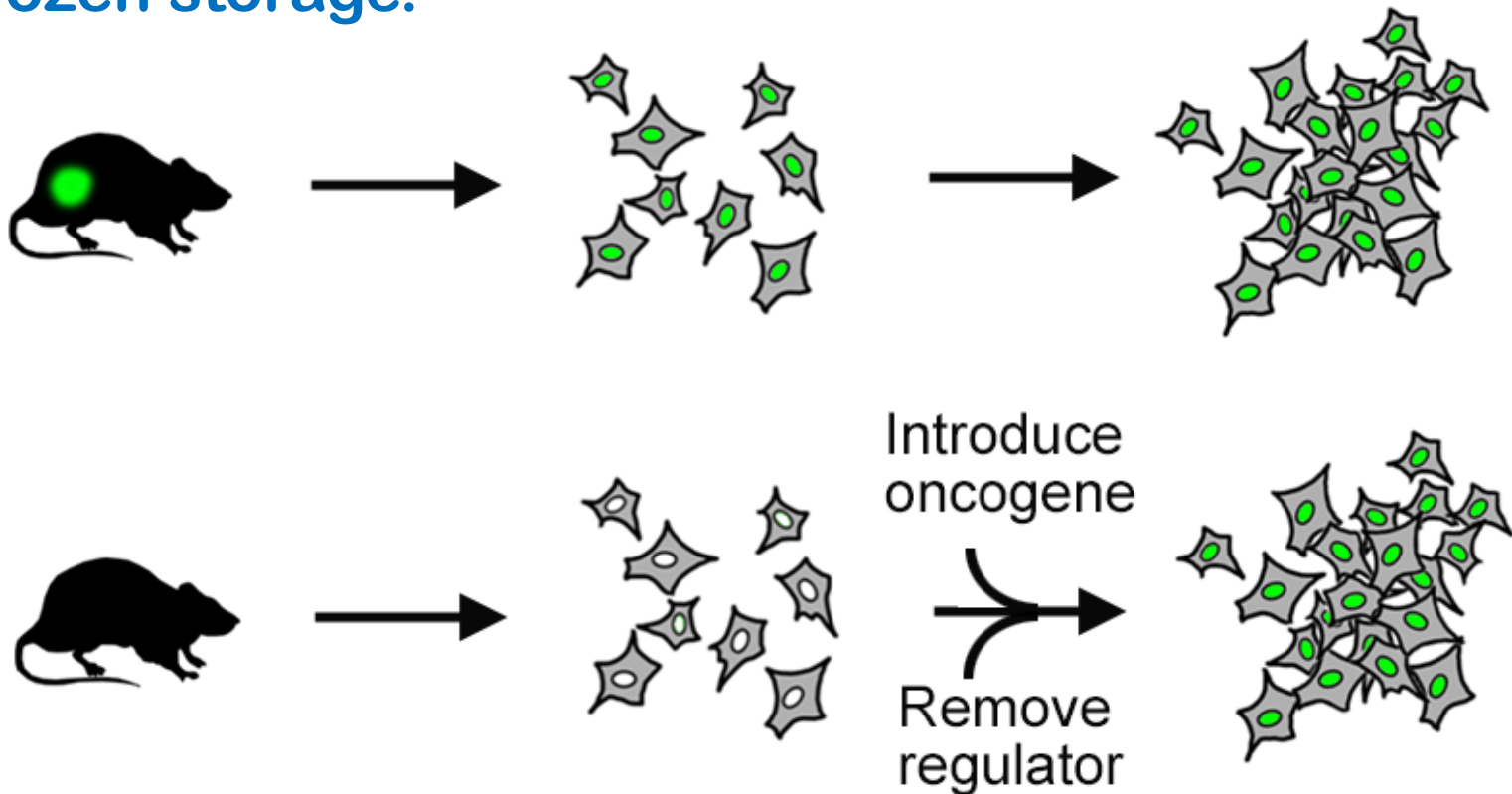
# Primary cells

Primary Cells (strains) are created by dissociation of tissue, have restricted growth, many properties of the original tissue type, and have limited capacity for frozen storage.



# Transformed cells

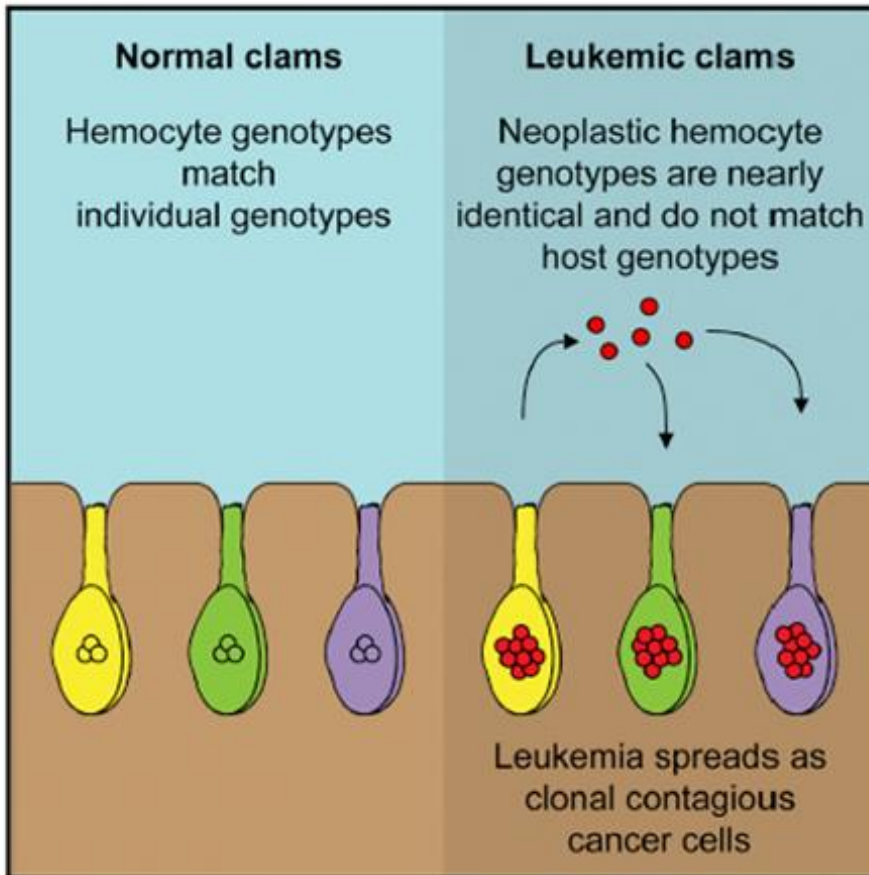
Transformed cells (lines) are produced from tumors or by direct modification of normal cells. They have unrestricted growth, are homogenous, and high capacity for frozen storage.



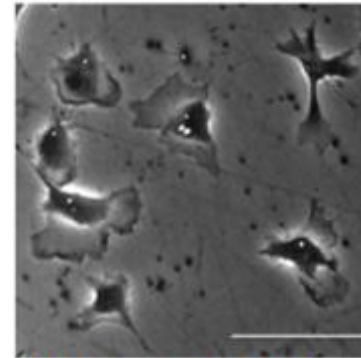
# Why are dreissenid cell lines important?

- They are crucial to a deep understanding of freshwater mussel physiology, and, because there is only one mollusk cell line (*Bge*), will add to our knowledge of mollusks in general.
- Cell lines will allow us to model the effects of environmental toxicants and stressors.
- Cell lines will accelerate the development of agents with the capacity to improve the health of native mollusk populations or to control invasive/pest populations.

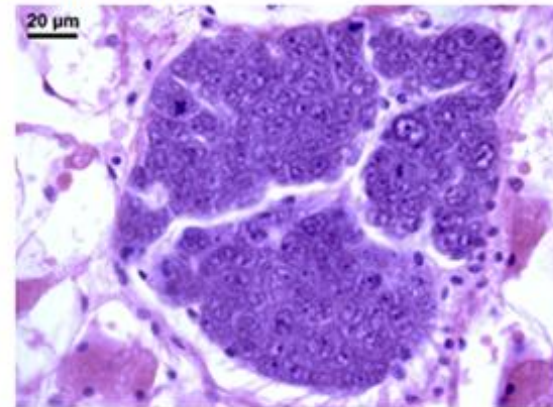
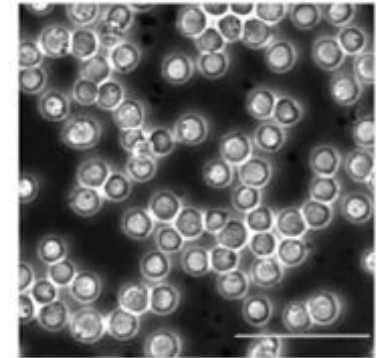
# Bivalve Disseminated Neoplasia



**Metzger et al. (2015)** Horizontal transmission of clonal cancer cells causes leukemia in soft-shell clams. *Cell*. 161:255-263



**Metzger et al. (2015)**

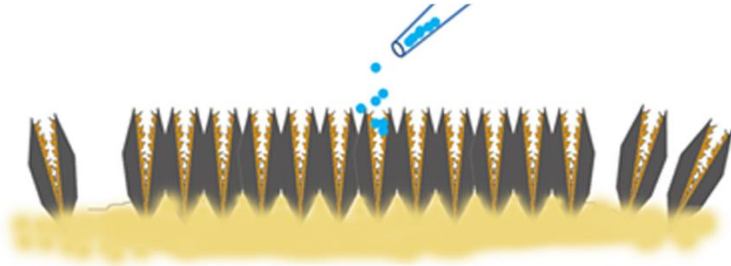


**Fig. 6.** Light micrograph of a histological section through the mantle of a mussel *Mytilus galloprovincialis* showing a gonad follicle filled with neoplastic cells.

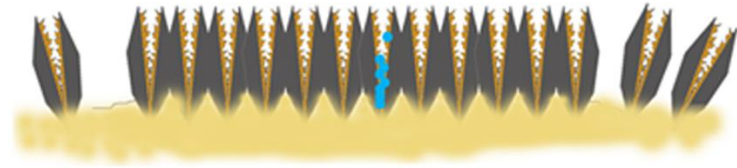
**Carballal et al. (2015)** Neoplastic diseases of marine bivalves. *J. Invertebr. Pathol.*; 131:83-106.

# Dreissenid cell lines may function as a disseminated neoplasia (DN)

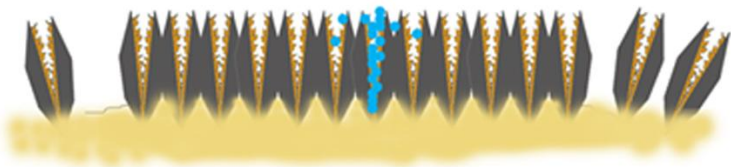
1. Deployment of the DN



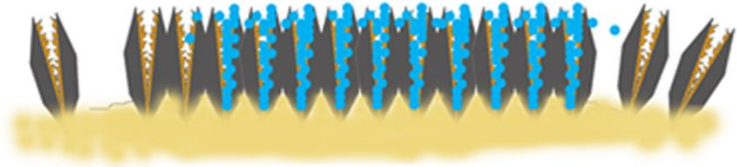
2. Engraftment to a live mussel



3. Development of systemic disease and early dissemination



4. Widespread dissemination to the target population



5. Population collapse in target waters





# A DN-based agent for invasive mussel control

- **Advantages:**

- Harmless to all plants, animals, and other organisms with the possible exception of closely related species (see below).
- Scalable to any size of water body and well-suited to deployment in open waters.
- Cost-effective and no special personnel/training required for deployment.
- Not a GMO: no potential for autonomous reproduction or life outside of a host mussel.
- Leaves no environmental footprint after invasive mussel population collapse.



- **Disadvantages:**

- Extensive testing will be needed to ascertain the impact on native bivalves. If toxicity is seen in some native species, re-engineering of DN lines may be needed minimize impact.
- High development (and testing) costs: estimated \$8.9M over 10 years to complete the project.
- Although not a GMO, there remains a risk of re-location and damage to zebra and quagga mussels in their native habitat.

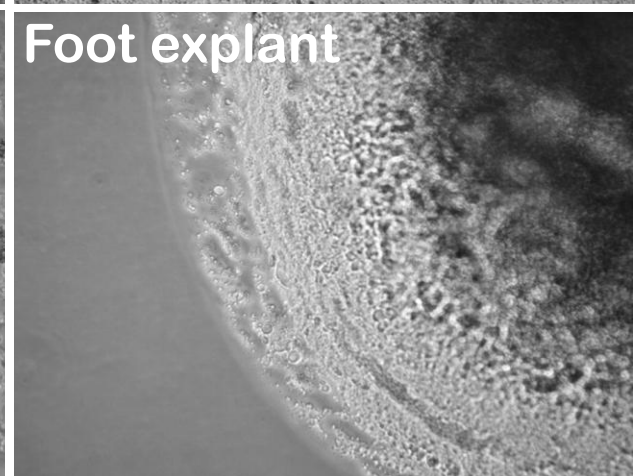
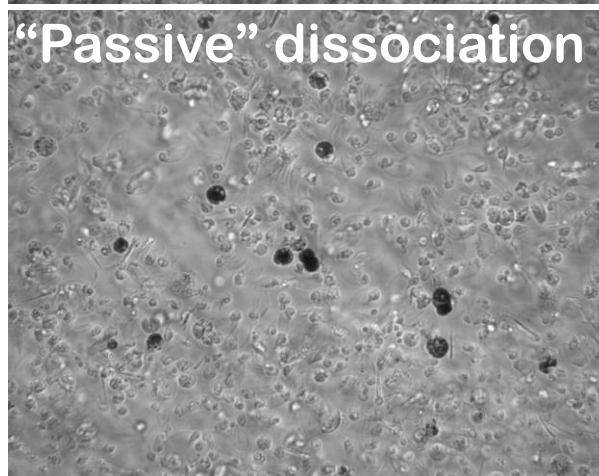
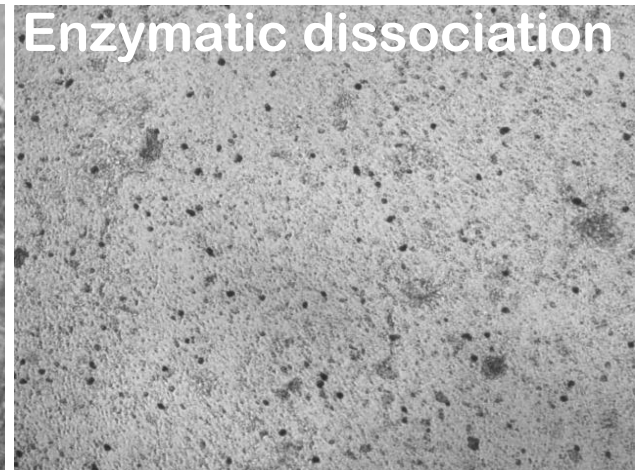
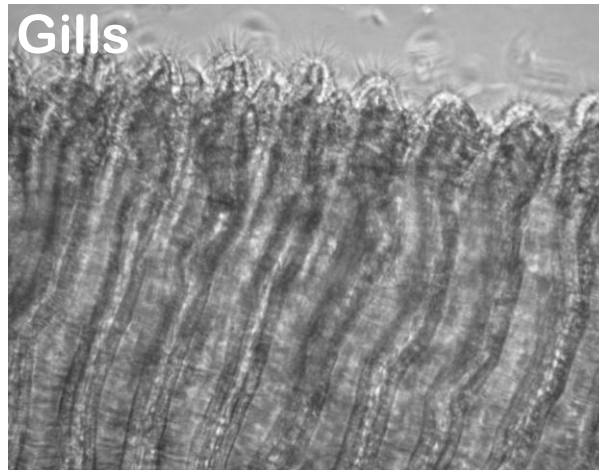
# Mussel aquaculture



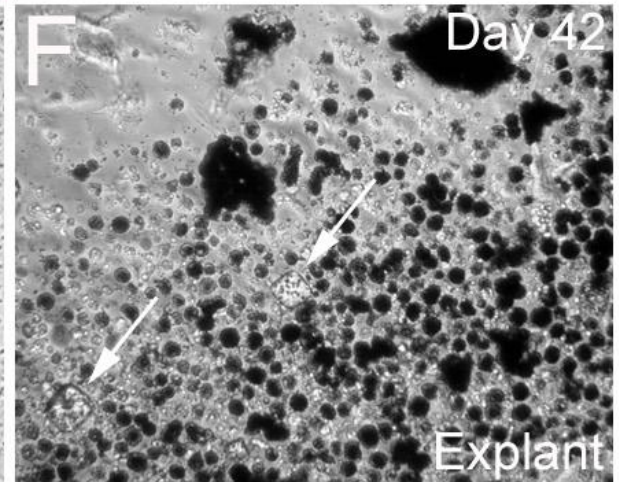
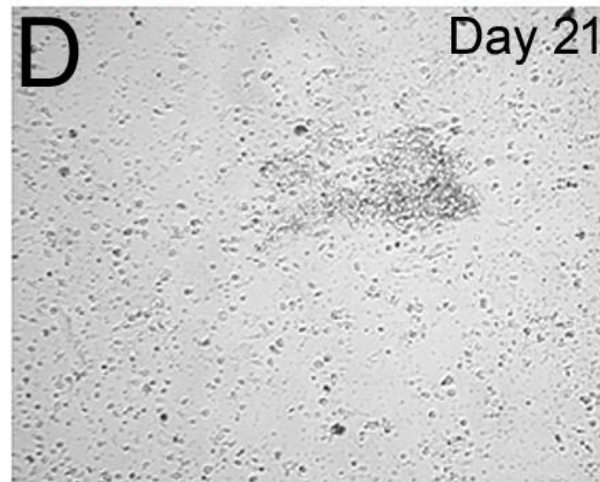
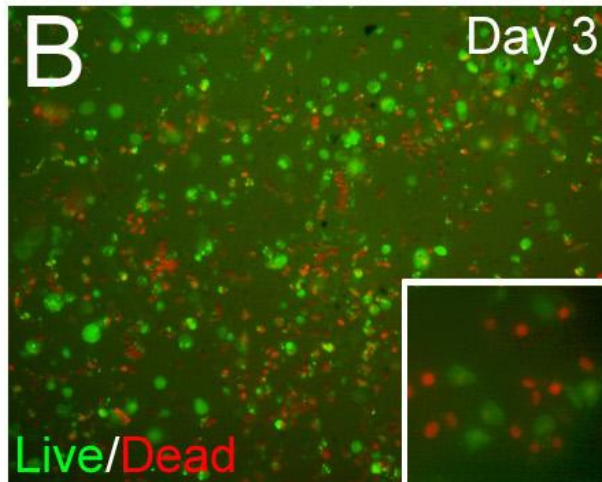
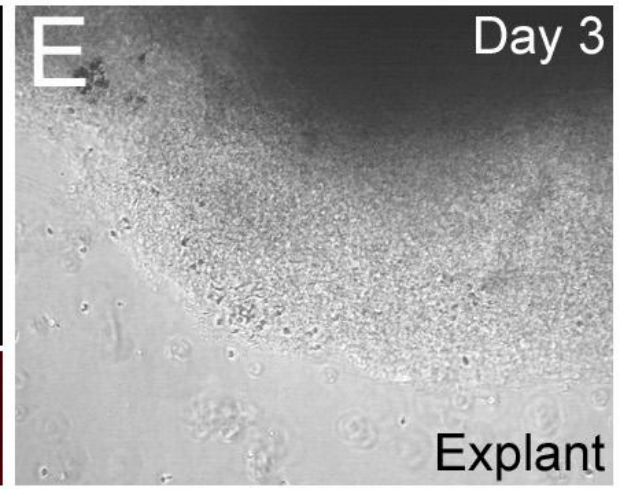
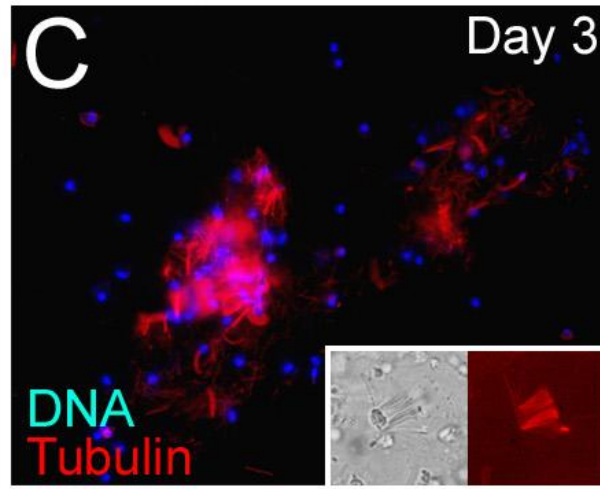
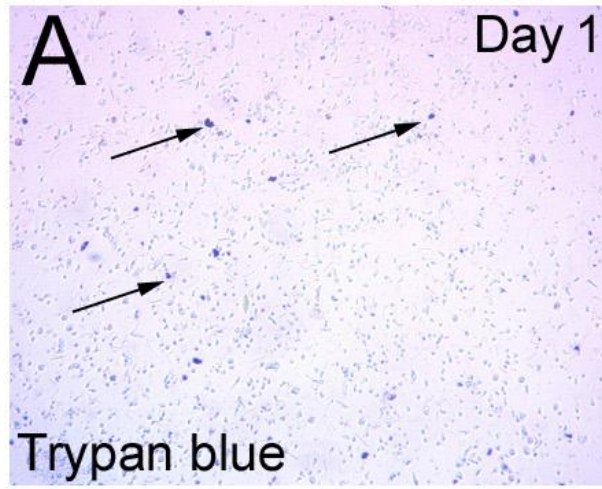
- Mussels sourced from Lake Michigan by NOAA, Muskegon MI
- Quaggas and zebras housed in-house since 2019 and typically for 11-12 months.
- Aerated dechlorinated tap water w/daily feedings. Water temperature 15°C.



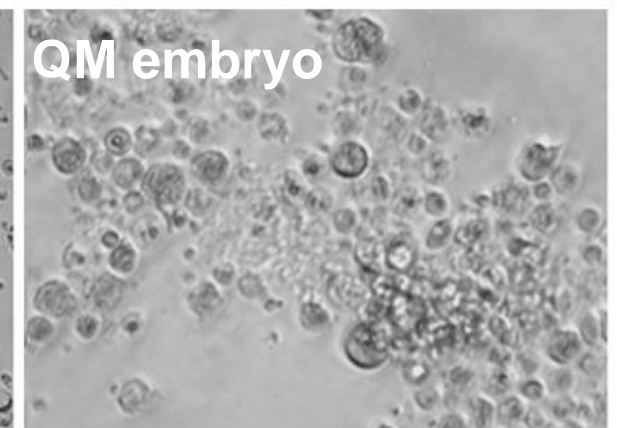
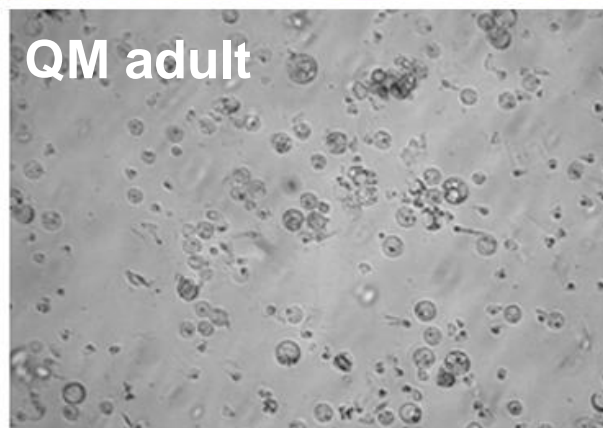
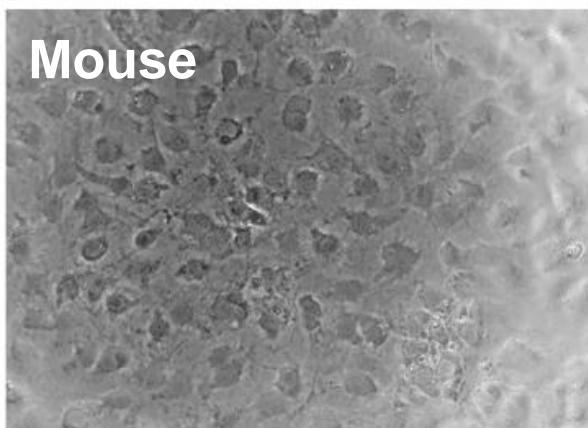
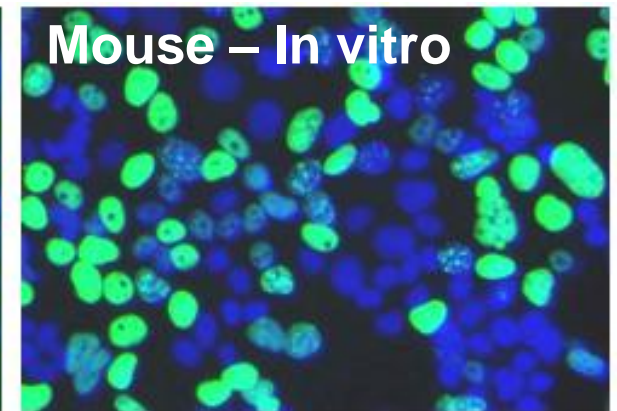
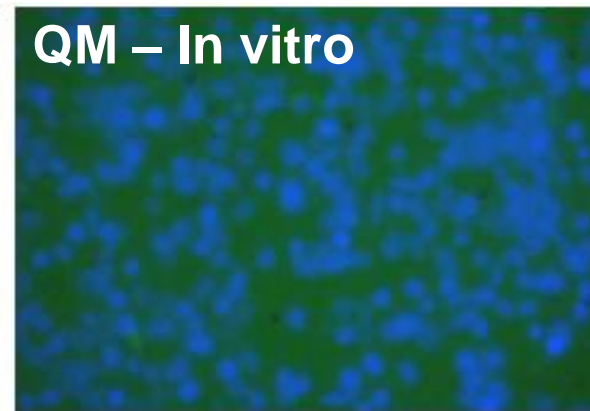
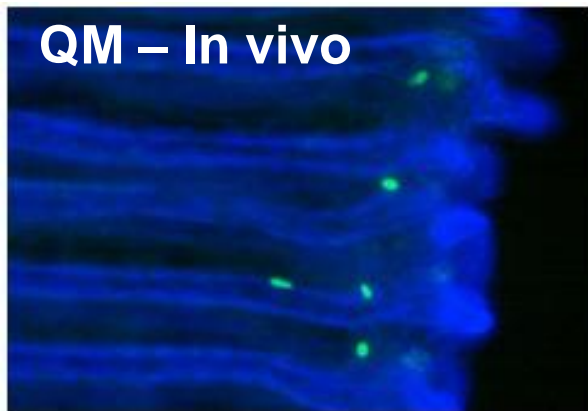
# *In vitro* culture of quagga -derived tissues and cells



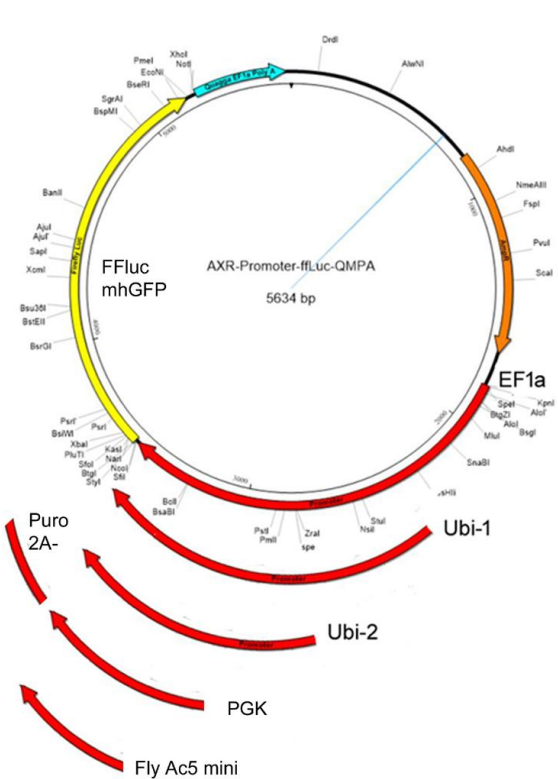
# Characterization of cultured cells



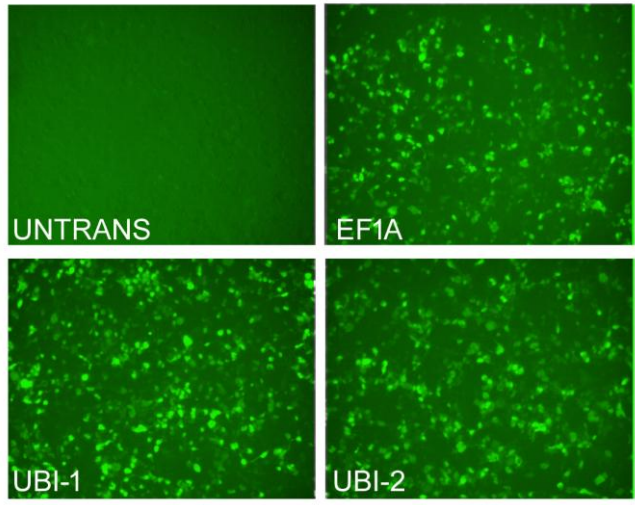
# Cultured QM cells do not divide or adhere



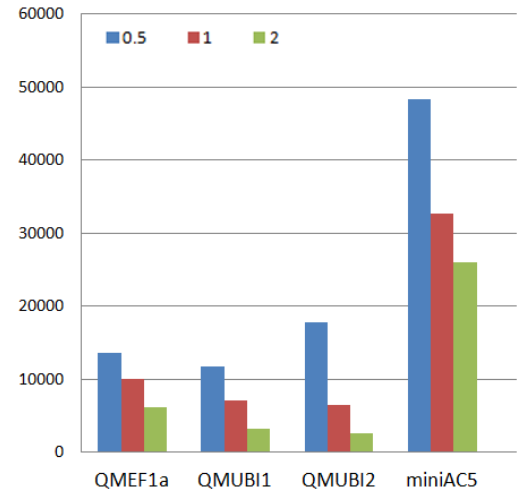
# Without mitosis, delivery of transforming factors to the nucleus of cultured cells would not occur.



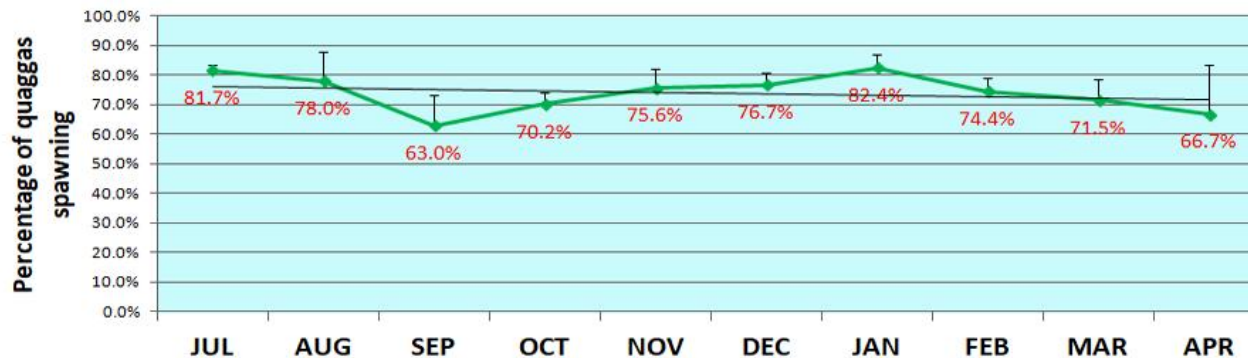
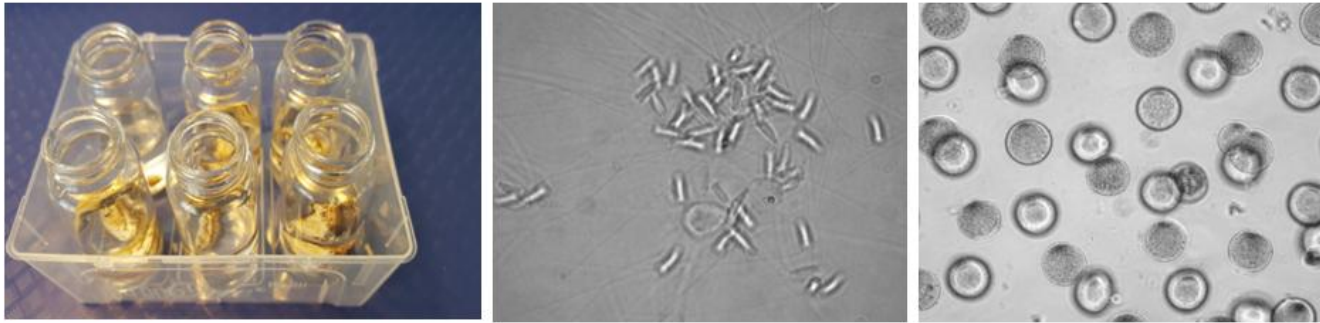
1 ug plasmid, HEK cells, D3-post



Drosophila S2 Cells

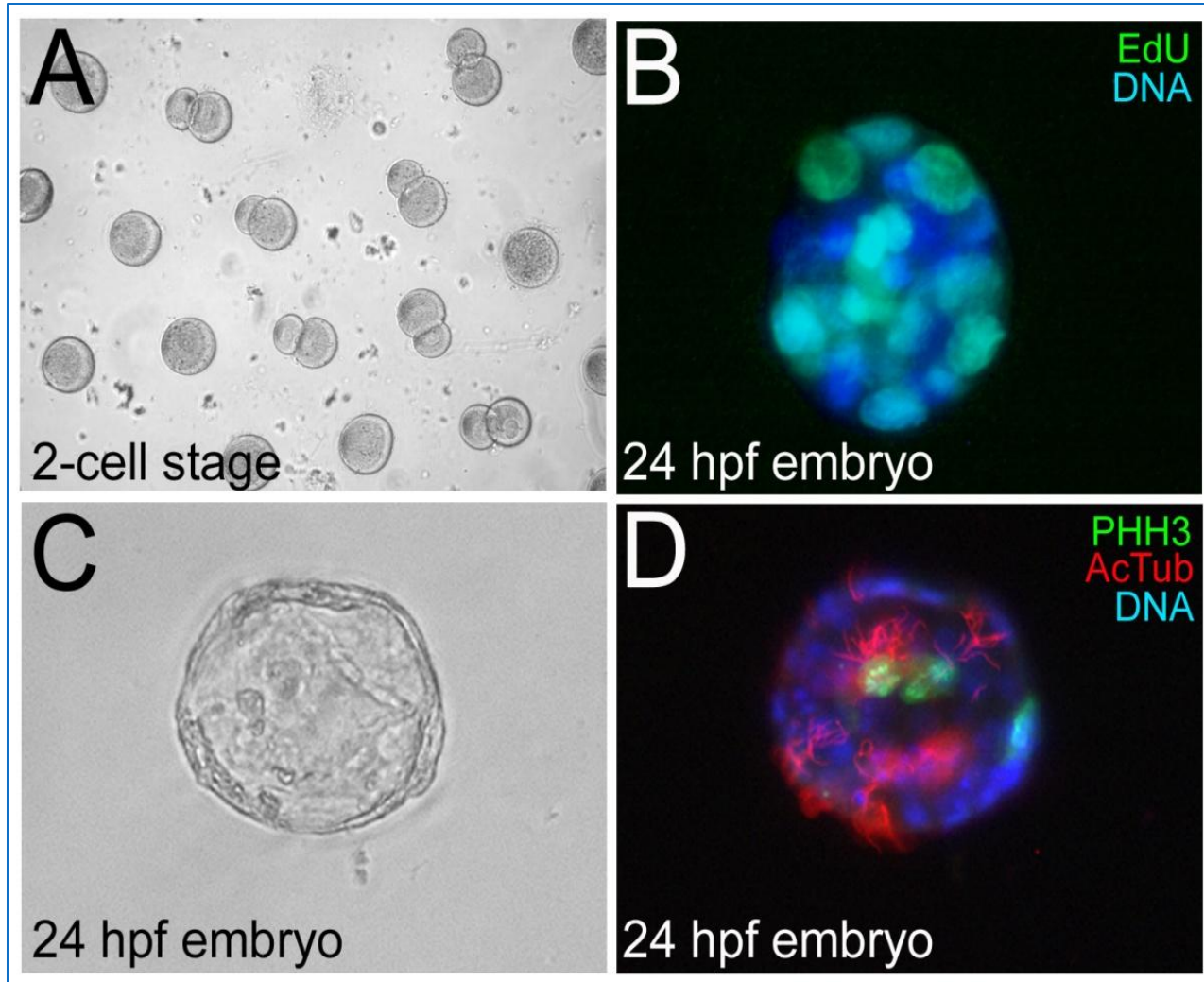


# QM embryo production

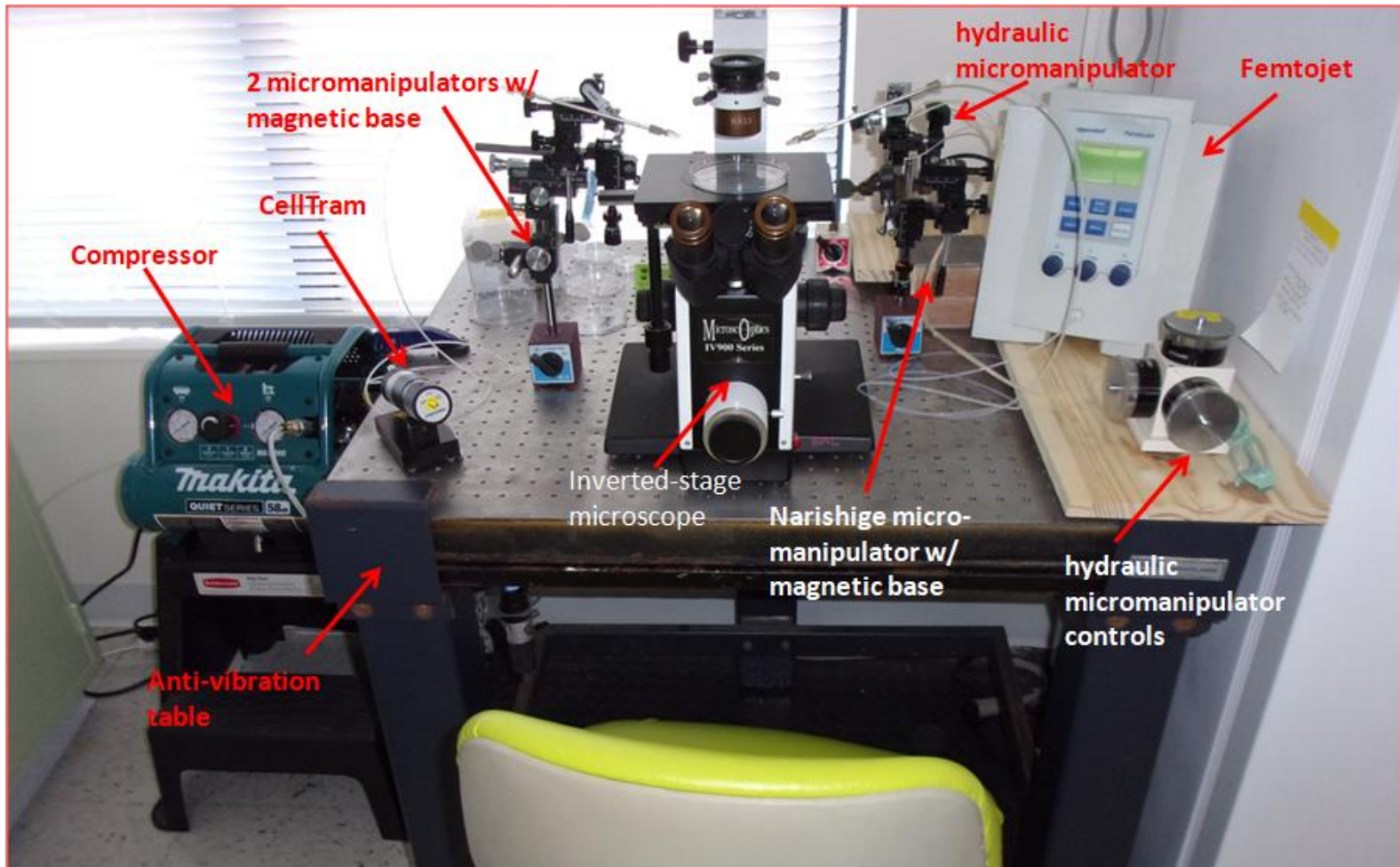




# Cell division and development of early QM embryos

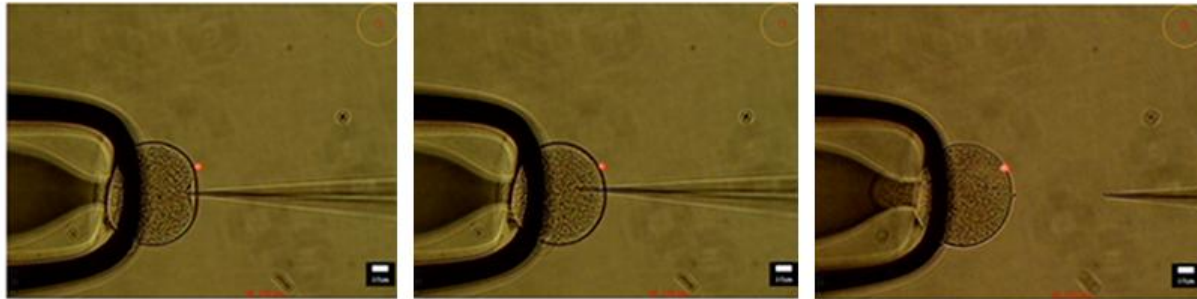


# Microinjection station completed in December 2022



# Currently, 0.5% of injected embryos develop after injection of mRNA

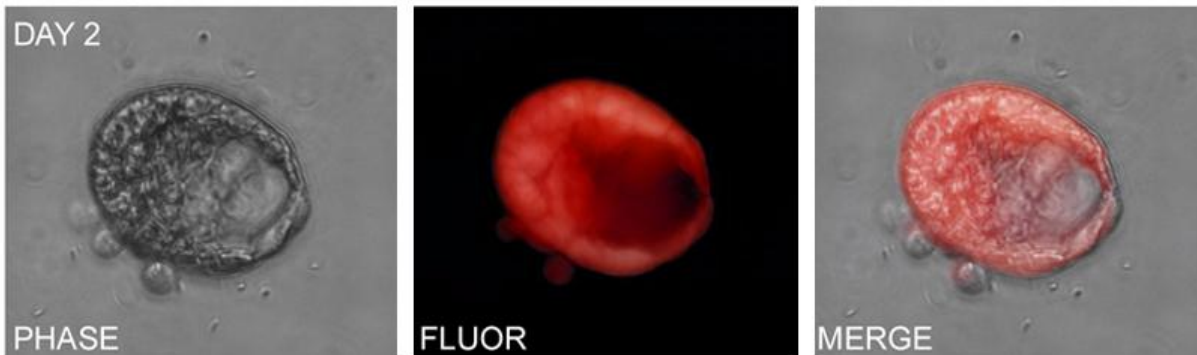
Injection  
(Day 0)



Post-injection  
Day 1



Post-injection  
Day 2



# Final thoughts...

- US BOR provides 100% of project funding, supporting two scientists and supplies.
- With successful introduction of nucleic acids achieved in February 2023, we hope to increase Biomilab personnel to 4-5 scientists to accelerate derivation and characterization of dreissenid lines and begin testing of the DN-based anti-mussel agent.
- Ideas for science or support? Please let us know at [office@biomilab.com](mailto:office@biomilab.com).
- Thank You!

# Project collaborators, consultants, and supporters



**Biomilab**  
Marie-Claude  
Senut  
Steve Suhr



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Sherri Pucherelli  
Jacque Keele  
Yale Passamaneck



Ashley Baldridge-  
Elgin

**IIMGB**  
Working  
Group

Many



Seth Herbst  
Lucas Nathan  
Tom Goniea

**EGLE**

Sarah LeSage



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Don Gerhart