Decoding Pregnancy Loss: Validating a Novel Genetic Biomarker of Poor Egg Quality

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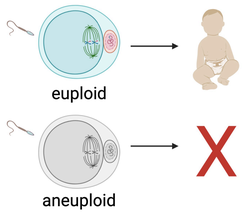
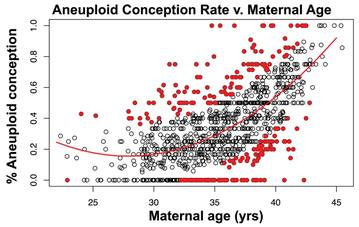
Background

***Aneuploidy*: the presence of an incorrect number of chromosomes in a cell, such as an egg.[1]**

- Egg aneuploidy is the leading genetic cause of miscarriage.[2,3,4]



- Currently, maternal age is the only biomarker for a patient's risk of ovulating an aneuploid egg.[3,4,5]



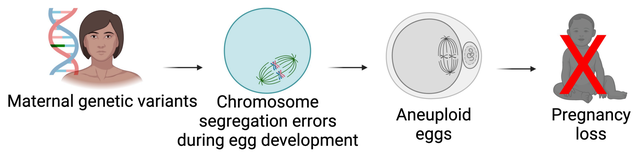
- However, some patients (● red dots in figure above) have higher or lower egg aneuploidy than predicted by maternal age alone.[6]
- For these patients, *age is an insufficient biomarker*.
- Genetic variants may account for age-disproportionate aneuploidy, but no genetic biomarker exists.[7]

RESEARCH OBJECTIVE

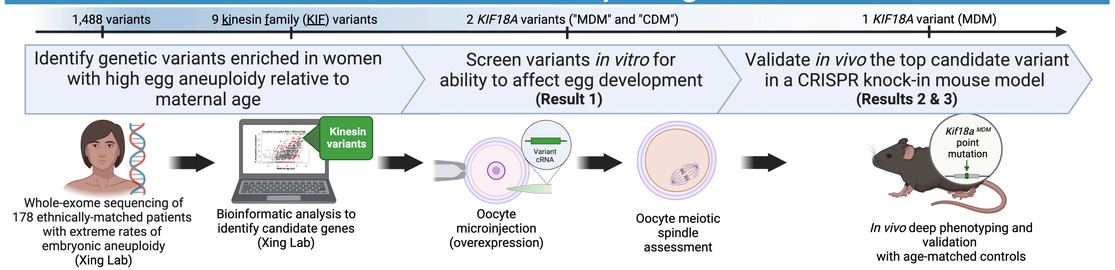
Identify causal genetic variants as predictive biomarkers of high egg aneuploidy relative to maternal age

Hypothesis

Maternal genetic variants cause age-disproportionate egg aneuploidy.



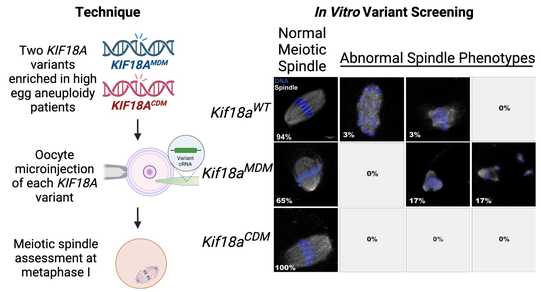
Methods: Study Design

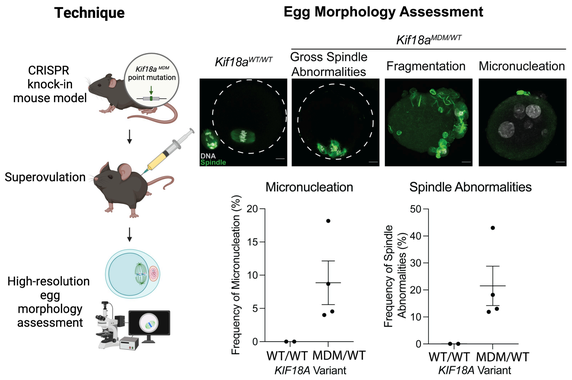


Results

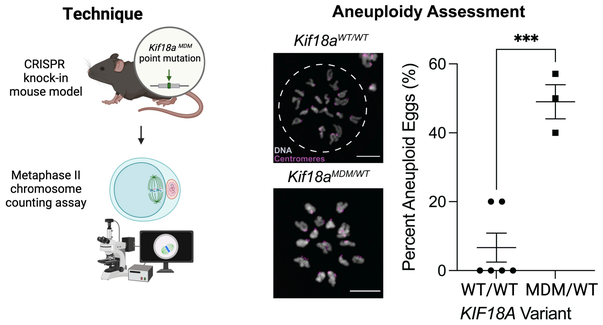
1. *In vitro* screening: *KIF18A*^{MDM} overexpression causes abnormal spindle formation in mouse oocytes.

2. *In vivo* phenotyping: *KIF18A*^{MDM} knock-in mice have abnormal egg morphology.



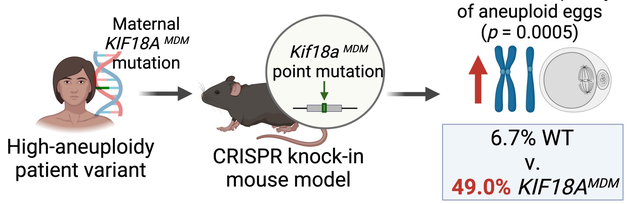


3. *In vivo* validation: *KIF18A*^{MDM} knock-in mice have increased egg aneuploidy.



Conclusions

KEY FINDING



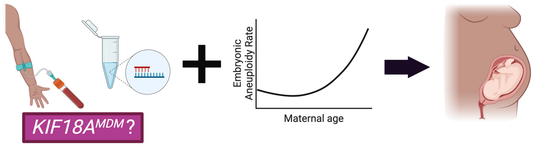
Summary of Study

- High egg aneuploidy patients → ↑ *KIF18A*^{MDM}
- *KIF18A*^{MDM} overexpression *in vitro* → ↑ meiotic spindle abnormalities
- *KIF18A*^{MDM} knock-in mouse → ↑ egg aneuploidy (p = 0.0005) + ↑ egg morphology abnormalities

Significance

Kif18a^{MDM} should be further studied as a novel potential biomarker for age-disproportionate egg aneuploidy.

Our Vision of the Future:
Precision Reproductive Medicine



Early genetic testing for predisposition to aneuploid eggs *prior to attempting to conceive*

Patient's age

Informed reproductive decision-making

Acknowledgements

This work was supported by NIH grant **R01HD091331** to KS and JX.
Leelabati Biswas is supported by NIH grant **T32GM139804** to Jerome Langer, Beatrice Haimovich, and Loren Runnels (2021-2022) and NIH fellowship **F30HD107976** to Leelabati Biswas (2022-2026).
Videographic support from Rutgers Academic Media.

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