

Mitochondrial Donation

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卵子核移植

卵子の細胞質・ミトコンドリアを交換することで、
ミトコンドリア病の伝播を回避する新しい治療法

ミトコンドリア提供: mitochondrial donation

ミトコンドリア置換: mitochondrial replacement therapy

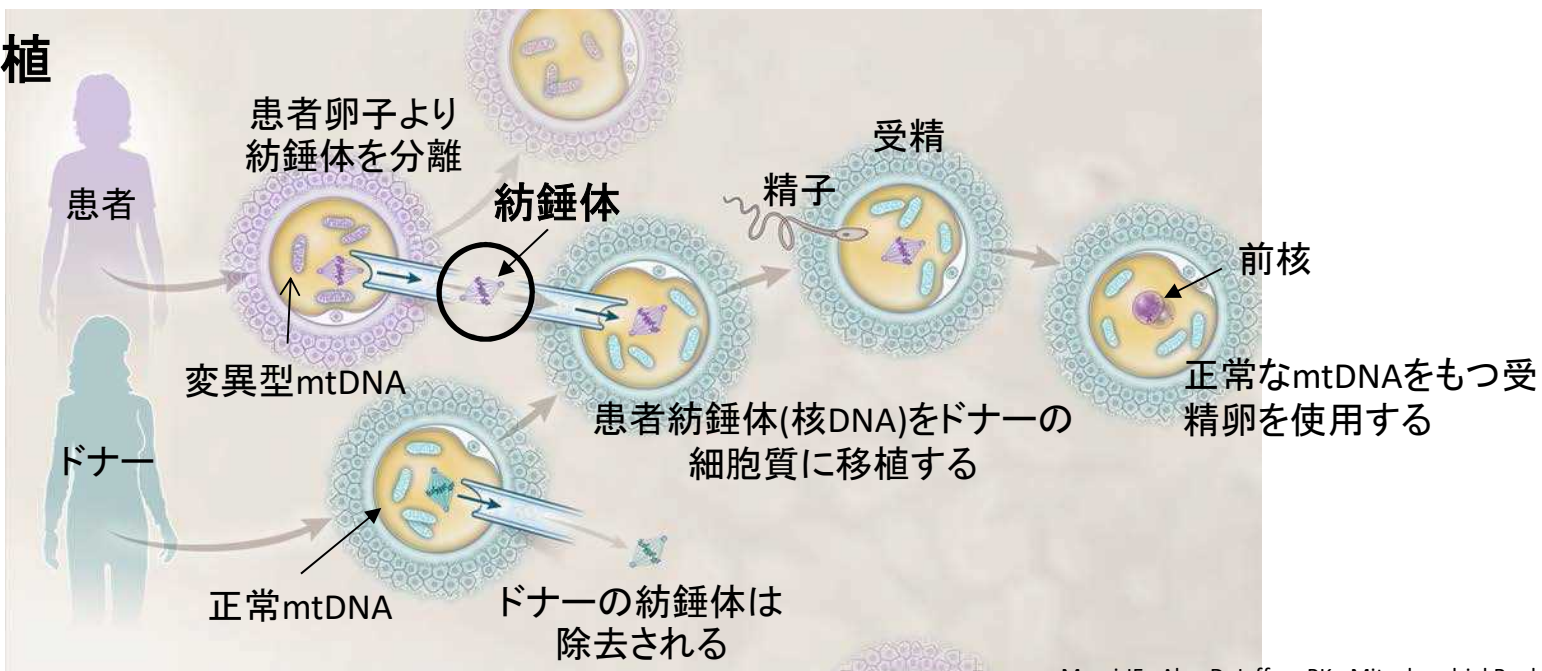
適応 ミトコンドリア遺伝子異常によるミトコンドリア病

きわめて高い変異率で発症する疾患 → Leigh脳症

方法 紡錘体移植: 卵子の紡錘体-染色体複合体を移植させる方法

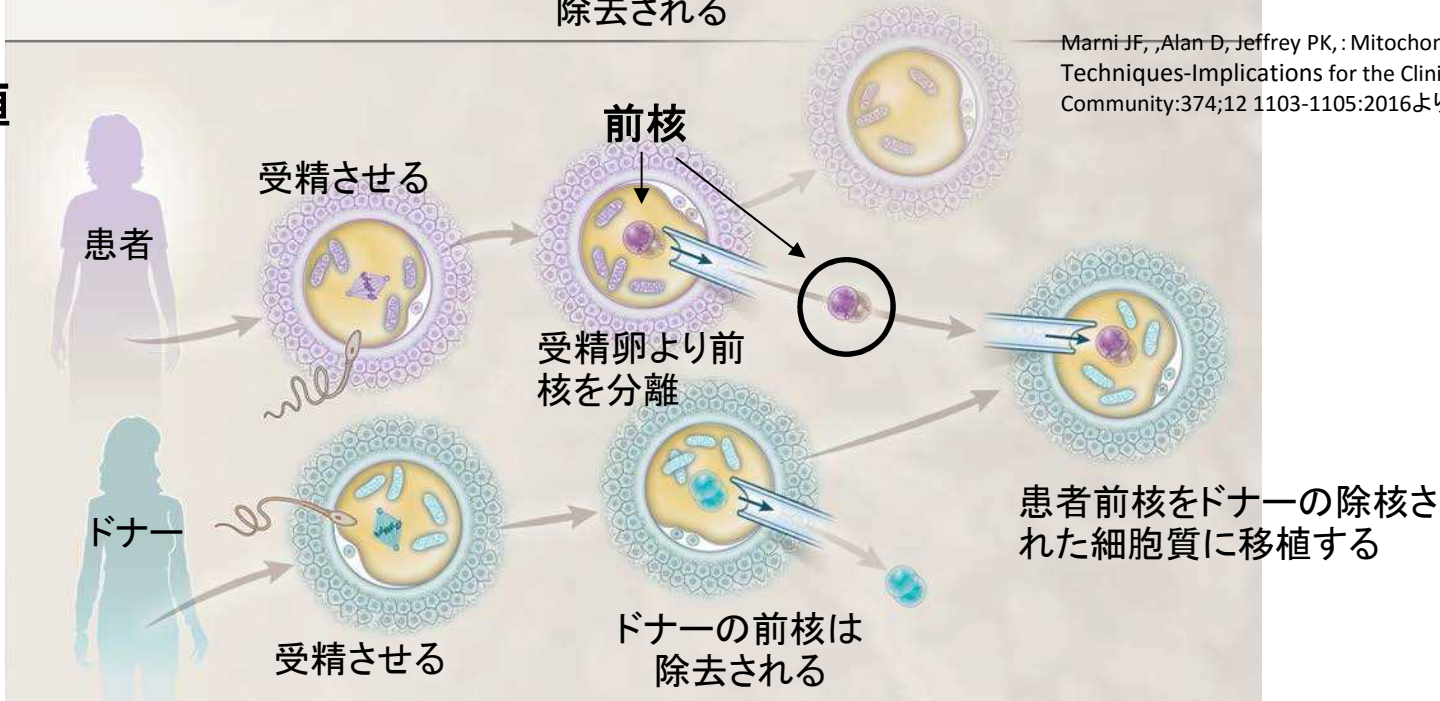
前核移植: 受精卵の雌性前核を移植させる方法

紡錘体移植 (MST)



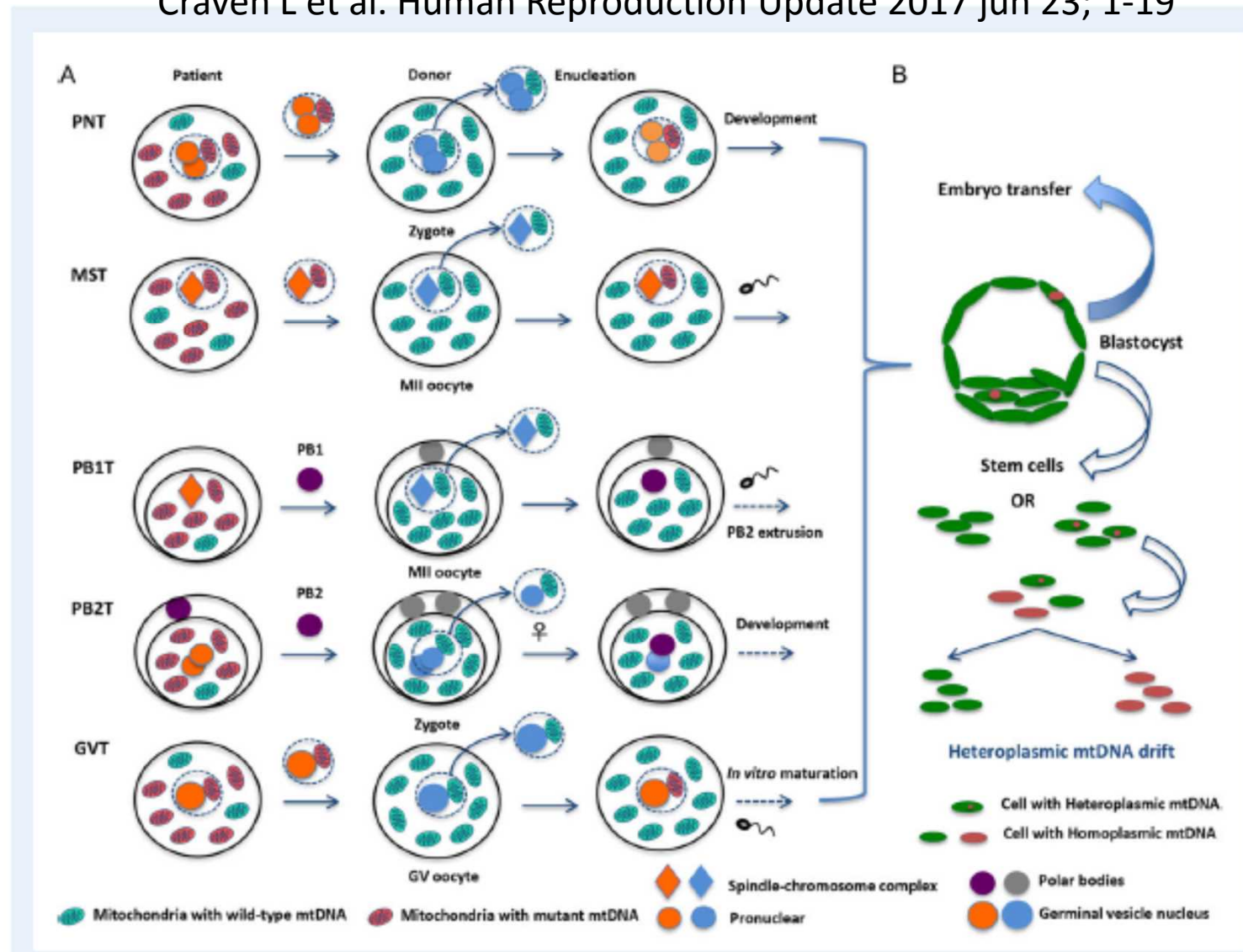
Marni JF, Alan D, Jeffrey PK, : Mitochondrial Replacement Techniques-Implications for the Clinical Community:374;12 1103-1105:2016より引用 一部改変

前核移植 (PNT)



There are 4 types of nuclear transfer techniques.

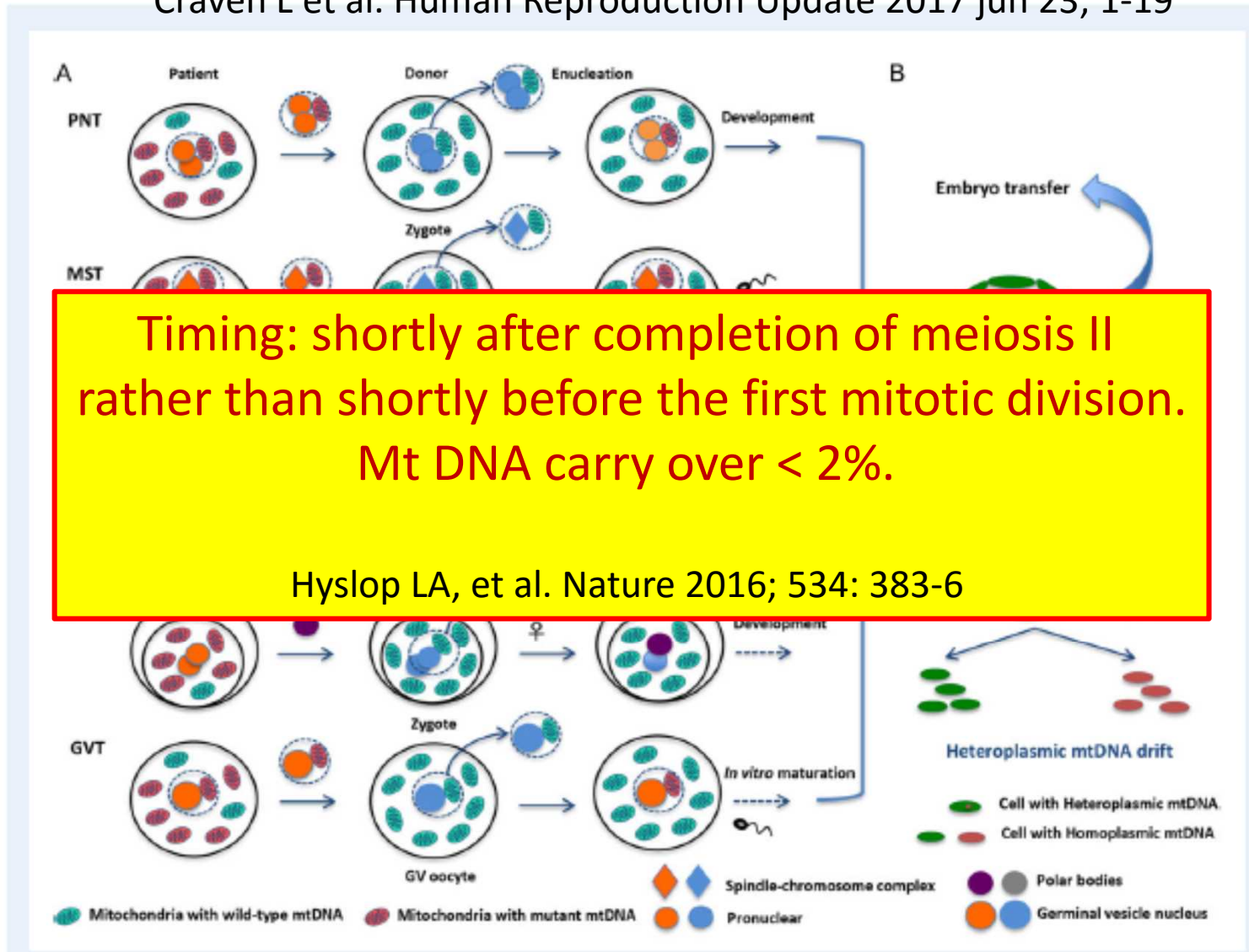
Craven L et al. Human Reproduction Update 2017 Jun 23; 1-19



PNT: pronuclear transfer, MST: maternal spindle transfer, PB1T/PB2T: first/second polar body transfer, GVT: germinal vesicle transfer

There are 4 types of nuclear transfer techniques.

Craven L et al. Human Reproduction Update 2017 Jun 23; 1-19



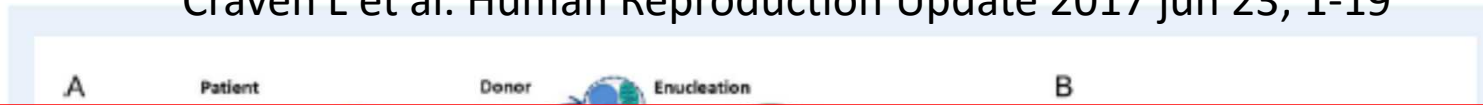
Timing: shortly after completion of meiosis II rather than shortly before the first mitotic division.
Mt DNA carry over < 2%.

Hyslop LA, et al. Nature 2016; 534: 383-6

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Sometimes, there occurs a mtDNA reversal, which may be related with mtDNA replication efficiency.

So, selecting the most compatible donor mtDNA should be important.

MtDNA carry over < 1%.

Kang E, et al. Nature 2016; 540: 270-275



Concerning the Zhang's first child with MST, mtDNA carry over is 5.73% at the stage of blastocyst, and 0 – 9.23 % in multiple organs after birth.

So, still uncertain the safety.

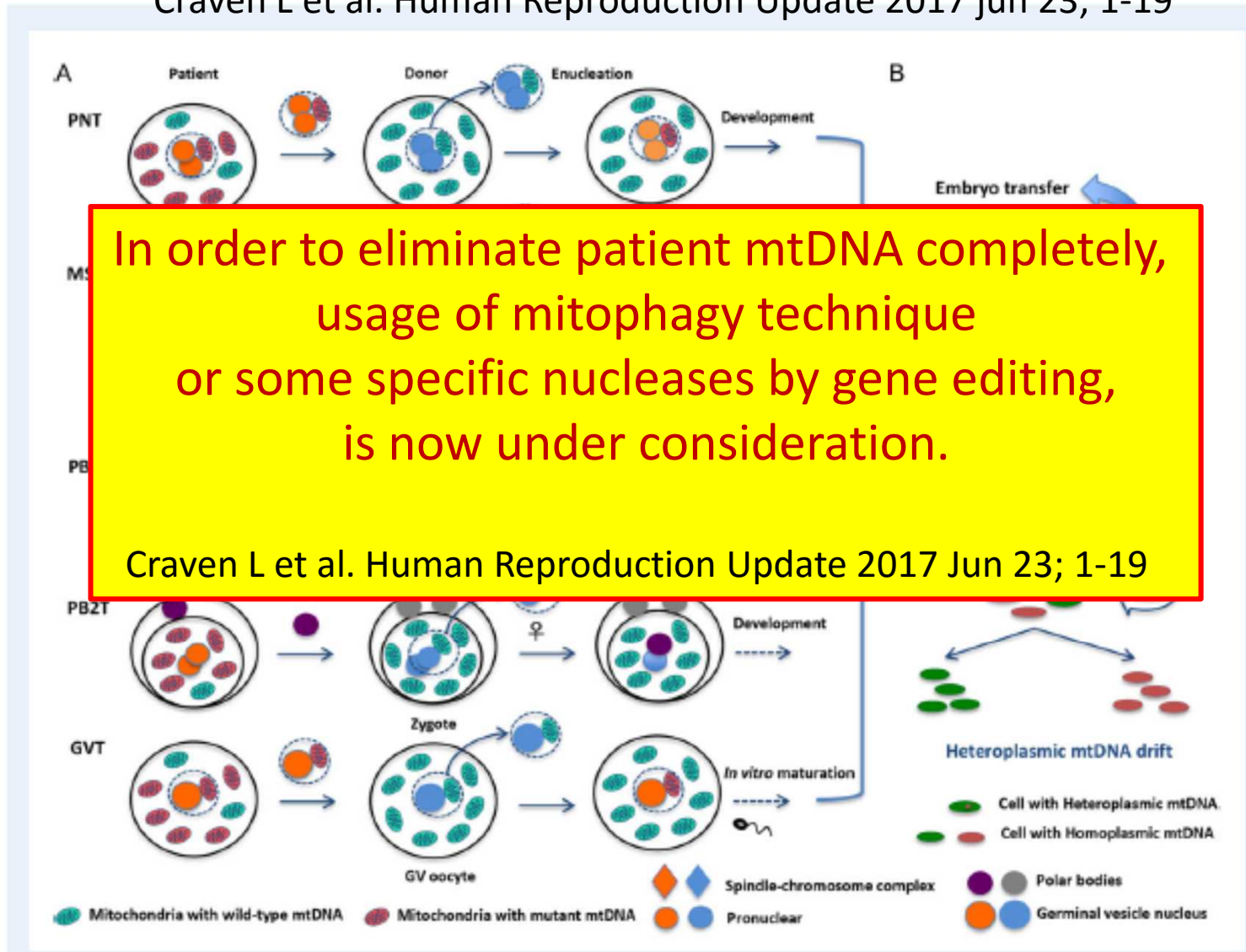
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Mitochondria with wild-type mtDNA Mitochondria with mutant mtDNA Pronuclear Germinal vesicle nucleus

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2015年 英国では法整備された

2016年 米国のグループが Leigh脳症保因者に紡錘体移植を行った文献
(ミトコンドリアDNA 8993T>G変異)

日本では卵子提供や生殖細胞への介入が法的に認められていない

問題点 倫理的な問題、法的・社会的な問題

次世代への影響

安全性、有効性についての検証が必要

→ エビデンスの蓄積、出生した児の長期的なフォローが必要

文献: John Z, Hui L, Zhuo L, et al: Live birth derived from oocyte spindle transfer to prevent mitochondrial disease. Reproductive biomedicine online 34:361-368,2017

A third MRT-baby is on its way

ETHICS in the NEWS, Oxford University Press, [January 22, 2019](#)

It has been [recently reported](#) (link in Spanish) that a 32 year old Greek woman is 27 weeks pregnant with a child who was conceived after a mitochondrial replacement technique (MRT) – in this case **Maternal Spindle Transfer (MST)**. If true this is really big news in terms of reproductive medicine and biotechnology, we are still waiting for data to be published. If successful, this would be just the *third birth* following a reproductive technique that *mixes the DNA of three people* (you will probably remember the big media buzz a couple of years ago about [‘three parent babies’](#)). This newest feat was achieved by a group of [Spanish](#) and [Greek](#) scientists; the clinical trial was carried out in Greece due to the fact that in Spain MRTs are not on the list of authorised reproductive techniques.

I attended a workshop on reproductive guidelines for mtDNA disease in Amsterdam on the way to Newcastle.

The Newcastle team are unable to release details of number of pregnancies (if any) or births and it sounds like they won't be able to do so for some time. This is because the families were worried about attracting lots of media attention so they have agreed to not announce when the first pregnancies and births occur.

I emphasised that it is very important for other countries to hear about results as soon as possible to enable it to proceed elsewhere and they seem to agree it would be appropriate to release results when a certain number of births have occurred so that the information is less identifiable.

They haven't decided what number of births that would be.

There is public information on the HFEA website apparently that so far there have been 13 licenses approved for mito donation.

That means 13 couples have had permission to enter the program but they can't/won't say what stage the couples are at.

Apr 8 from Prof. David Thorburn MCRI, Melbourne, Australia