

Congrès meetchondrie

9-12 Mai 2010 Aussois



*meet*chondrie

MeetOchondries



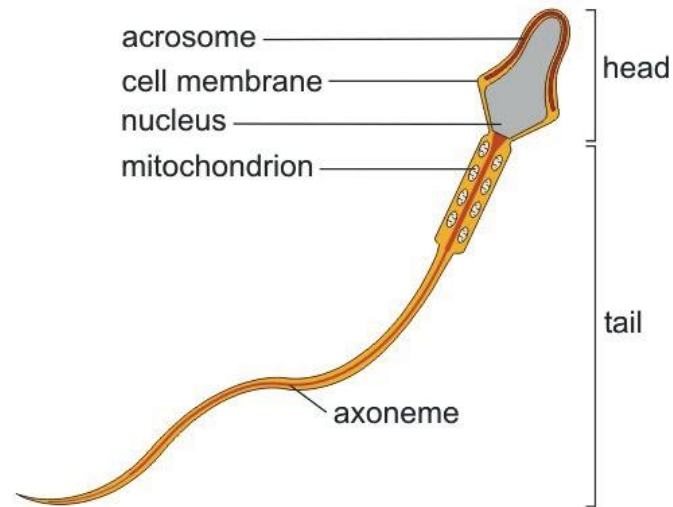
et (in)fertilité
mâle

Philippe Marchetti

CHU Lille
Inserm U837

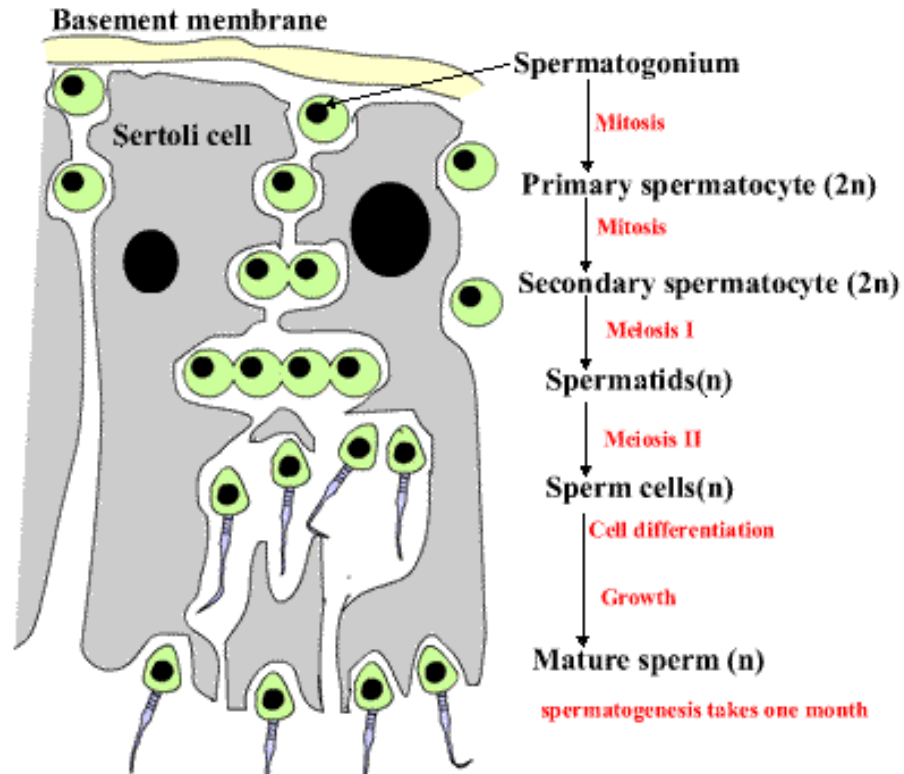
Mitochondries des spermatozoides importantes pour fertilité ?

Morphologie du spermatozoïde

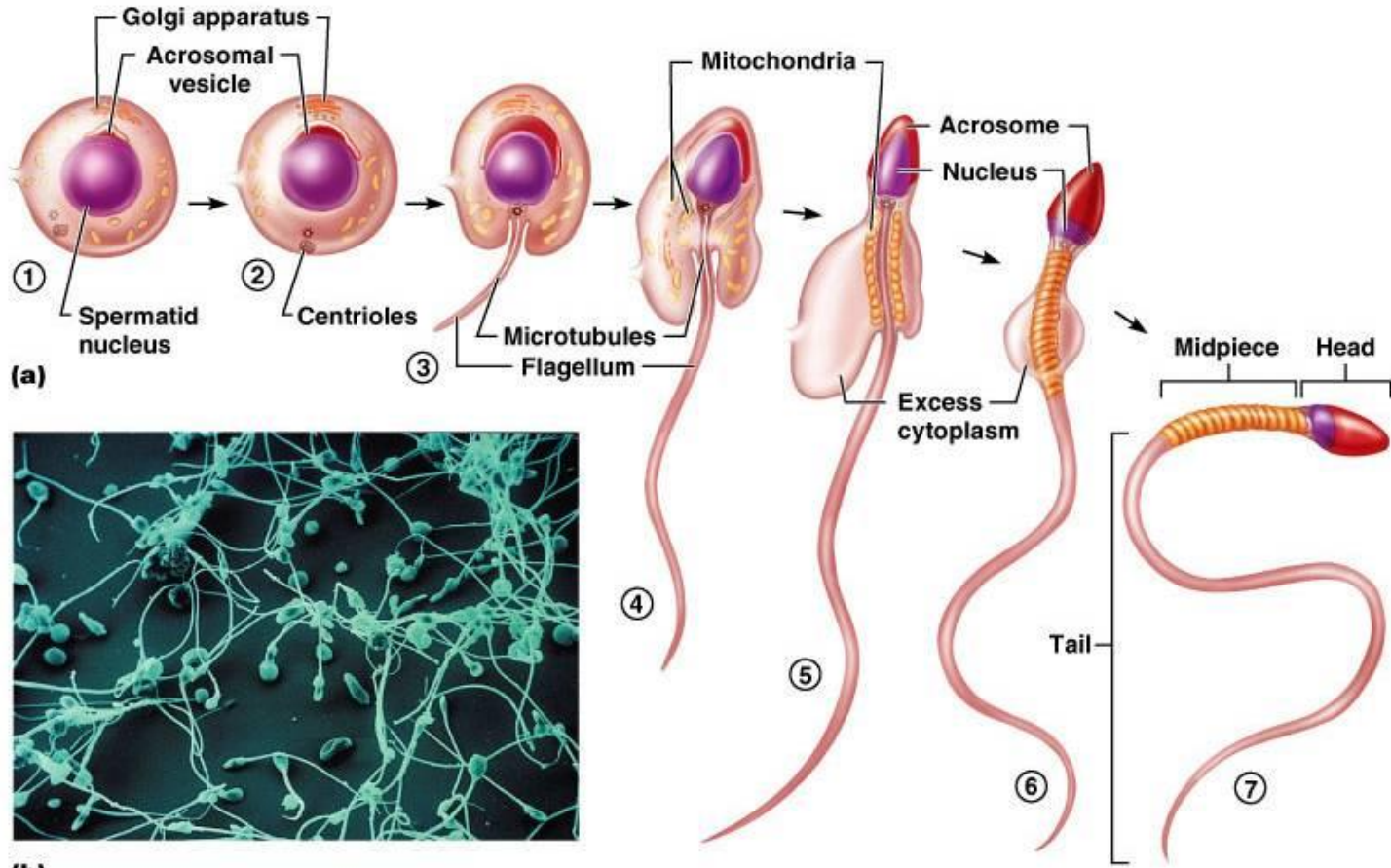


Spermatogenèse produit les spermatozoïdes matures

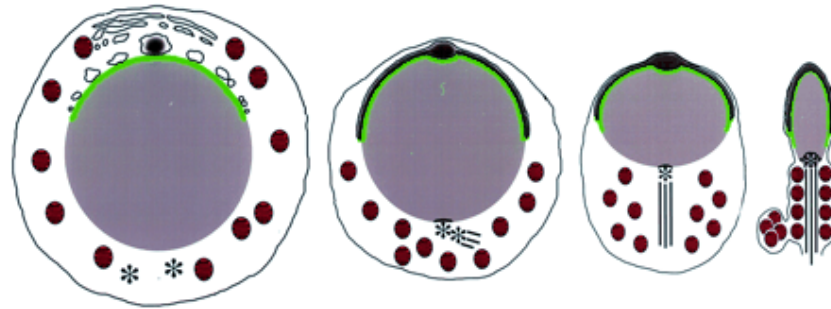
Les tubes séminifères



Spermatogenèse produit les spermatozoïdes matures

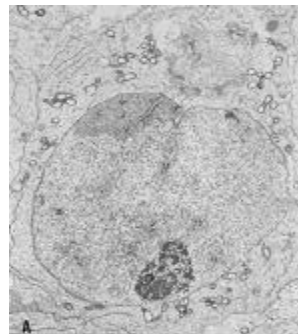
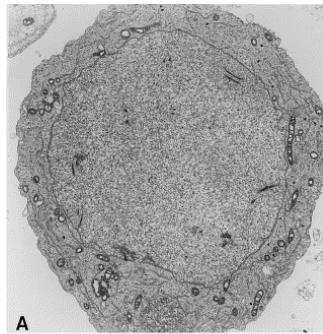


Mitochondries et spermatogenèse



Mitochondria
Perinuclear theca
Acrosome

Centrioles **
Axoneme ≡
Nucleus



A

Germ cell type

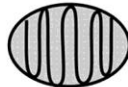
Spermatogonia
 Preleptotene spermatocyte
 Leptotene spermatocyte

Zygotene spermatocyte

Pachytene spermatocyte
 Secondary spermatocytes
 Early Spermatids

Late spermatids
 Spermatozoa

Mitochondria



Orthodox



Intermediate

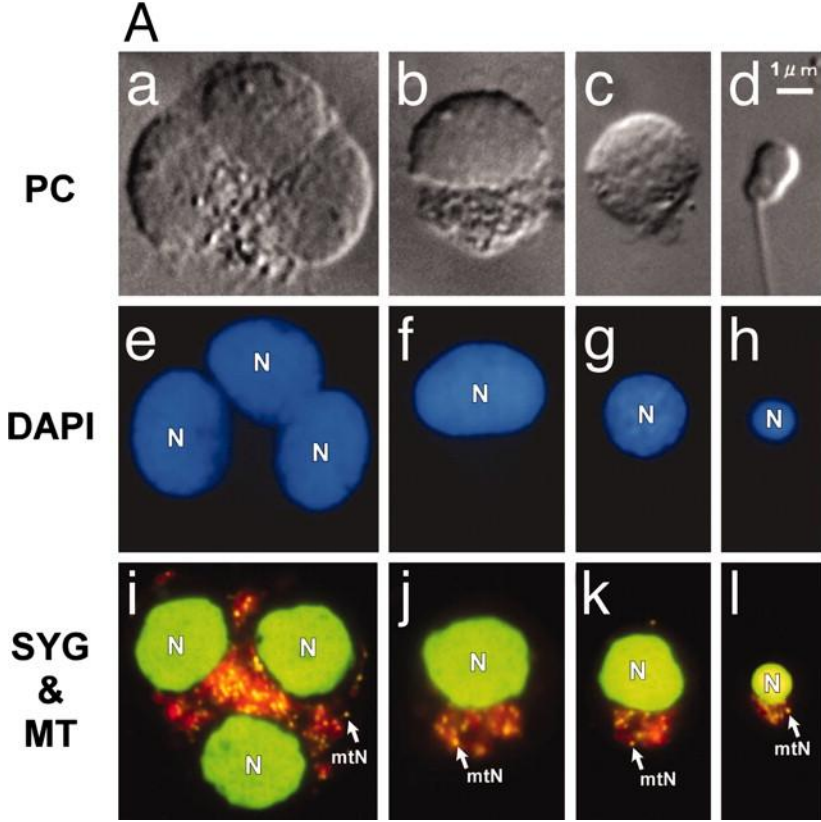


Condensed



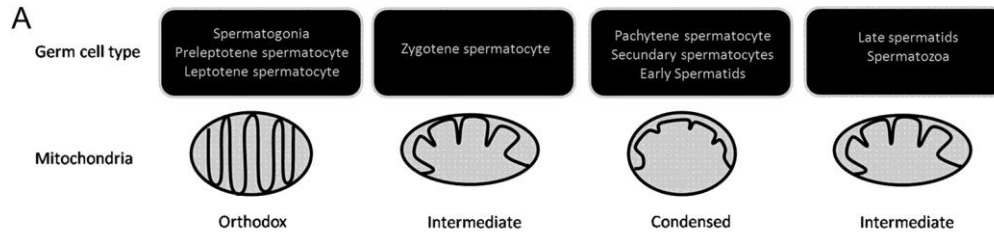
Intermediate

Réduction ADN mt lors de la spermatogenèse

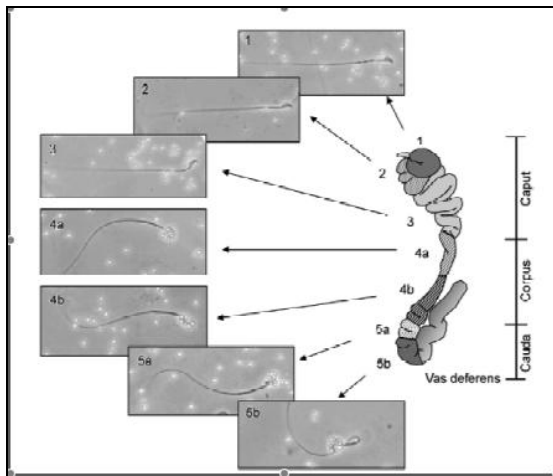


Nishimura Y et al. PNAS 2006;103:1382-1387

Mitochondries et spermatogenèse



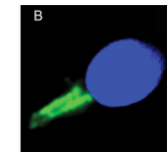
D'après Meinhardt et al.



Mitochondries silencieuses

Activité COX

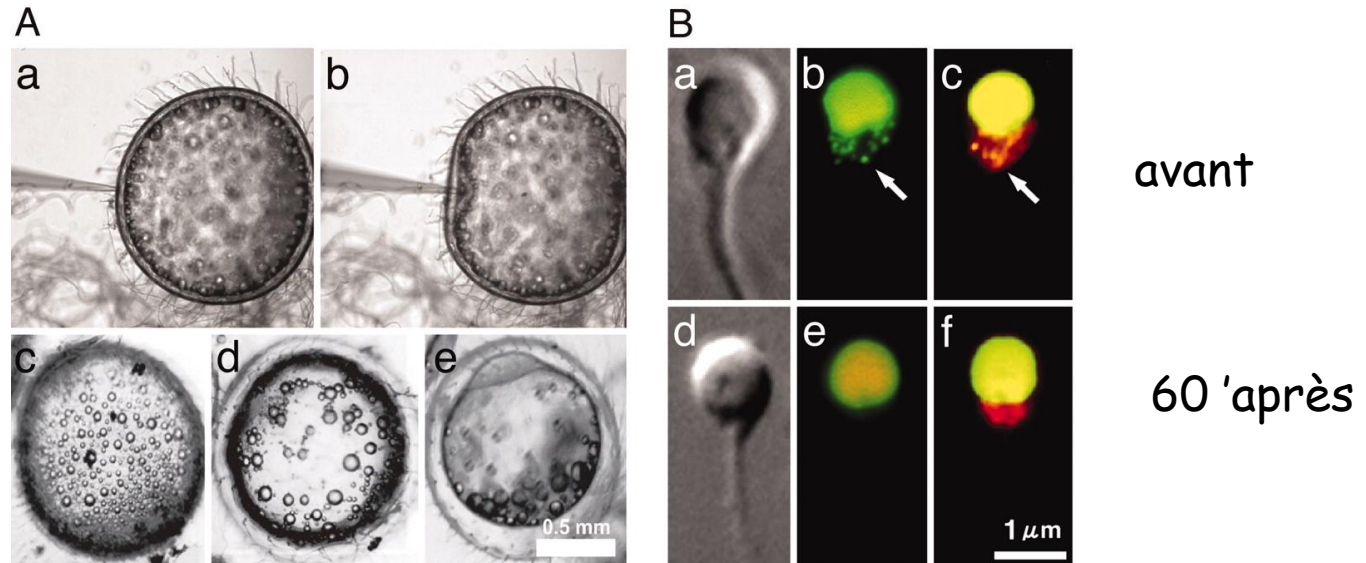
$\Delta\psi_m$



Mitochondries fonctionnellement actives

Mitochondries des spermatozoïdes inutiles au développement embryonnaire

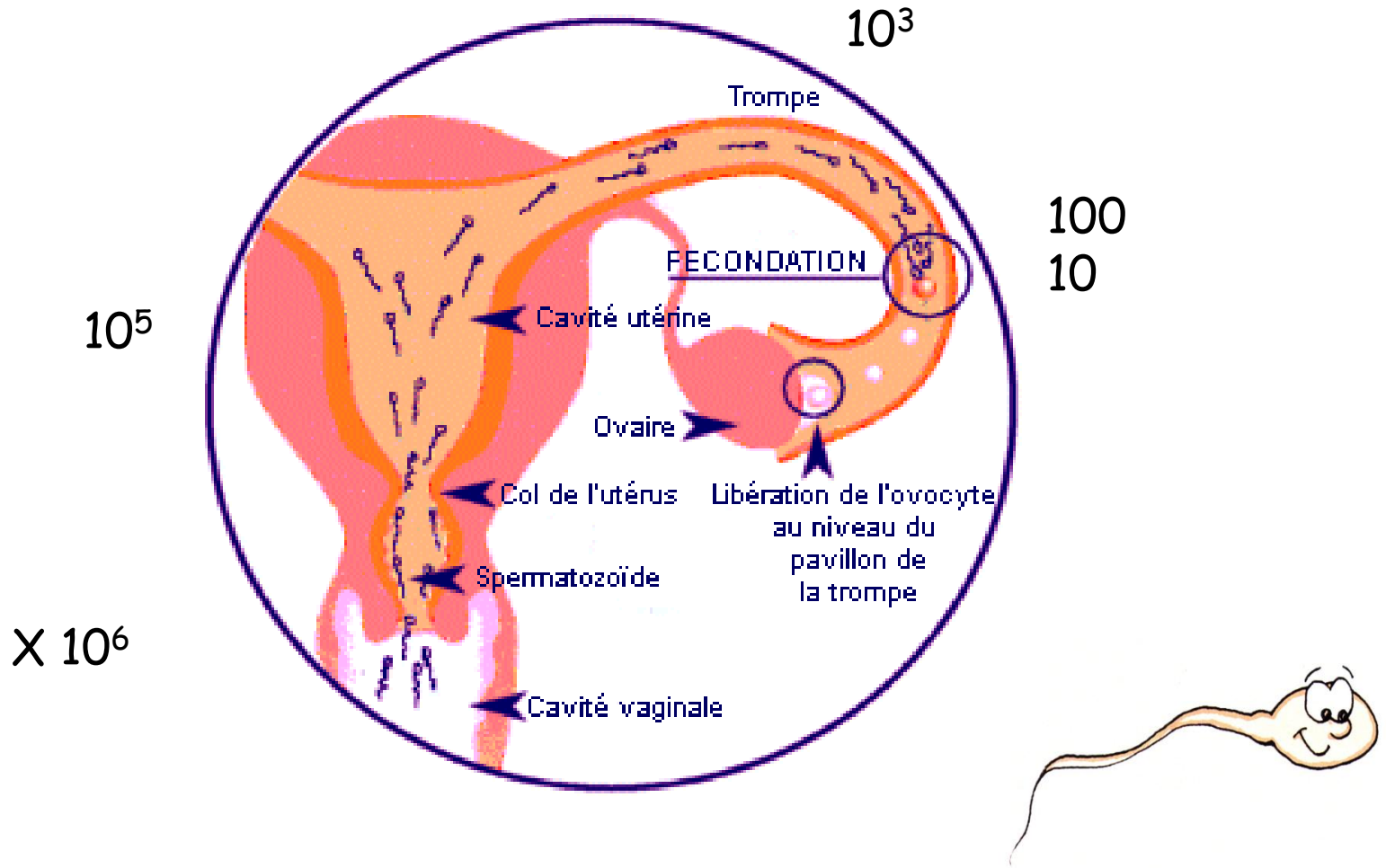
Active digestion of sperm mtDNA after injection into eggs.



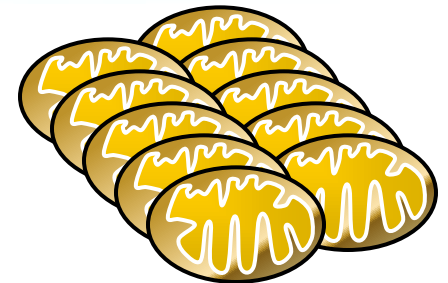
Nishimura Y et al. PNAS 2006;103:1382-1387

Si Mitochondries des spermatozoïdes importantes pour fertilité..
.....avant fécondation

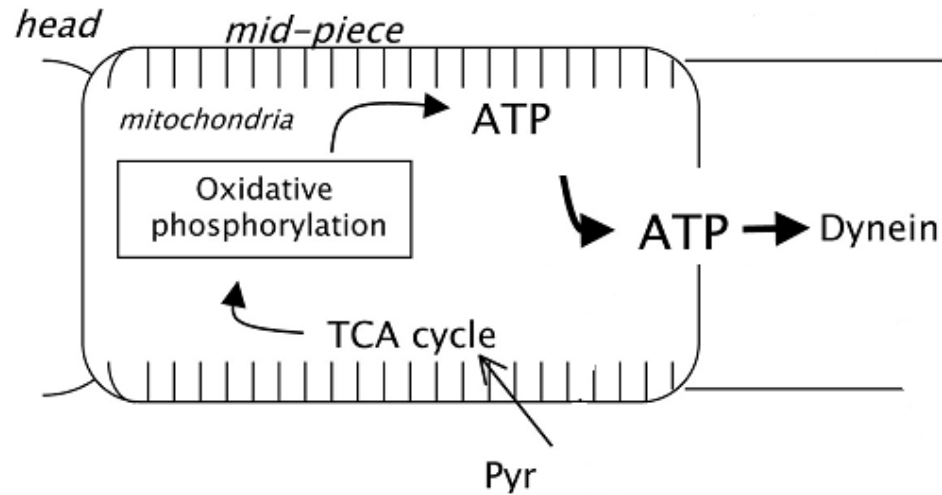
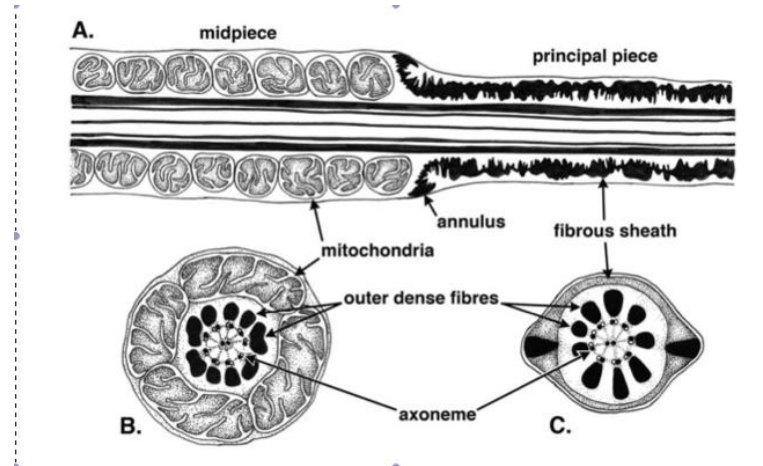
Compétition des spermatozoïdes pour féconder l'ovocyte



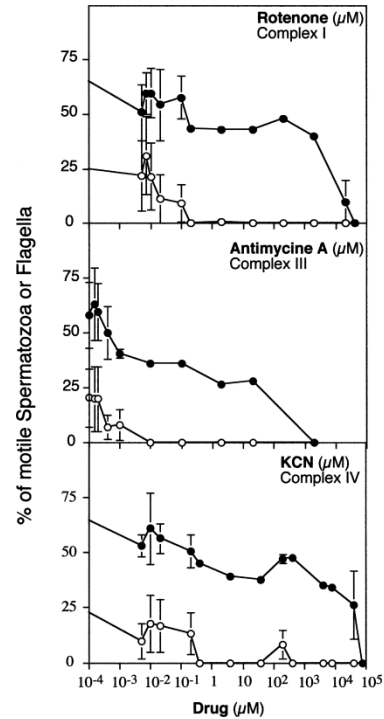
Le critère qualitatif majeur du spermatozoïde est sa mobilité



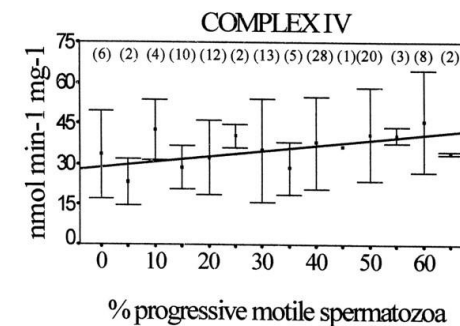
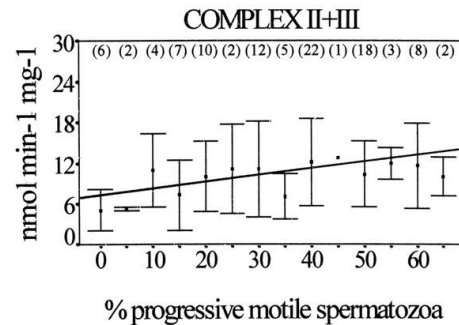
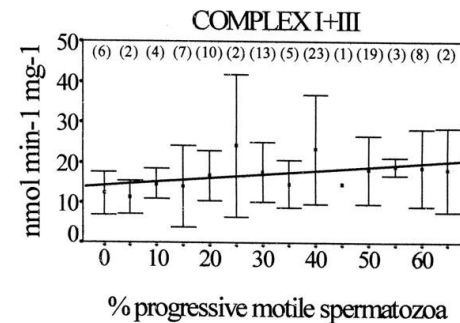
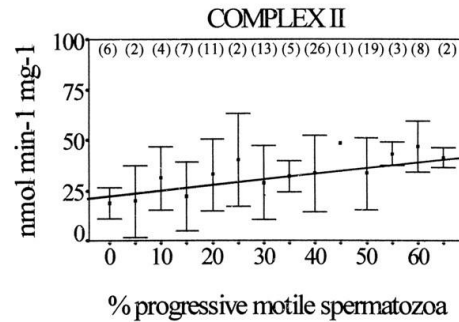
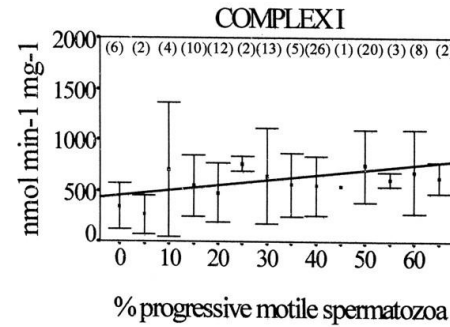
la mobilité des spermatozoïdes implique les mitochondries



Mobilité des spermatozoïdes dépend de l'activité des complexes

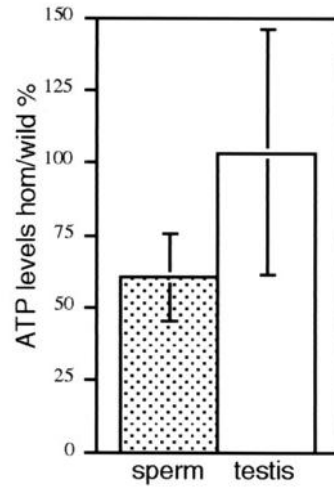


Correlation between sperm motility and specific activities in spermatozoa

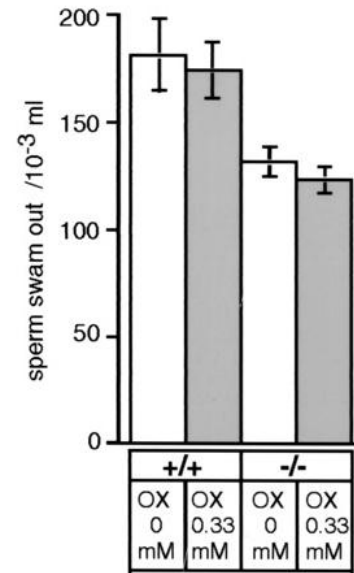


Les souris *cyt-c^t* KO ont des spermatozoïdes peu mobiles

B



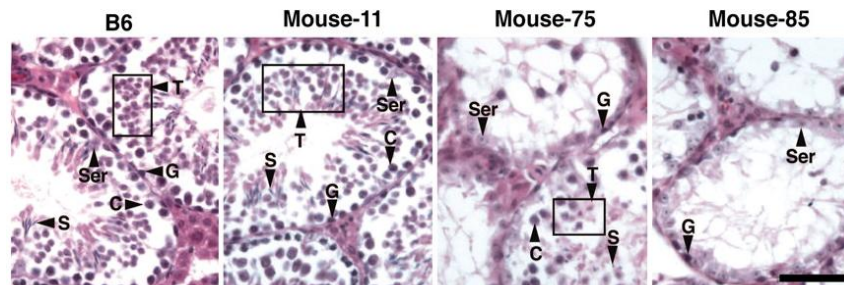
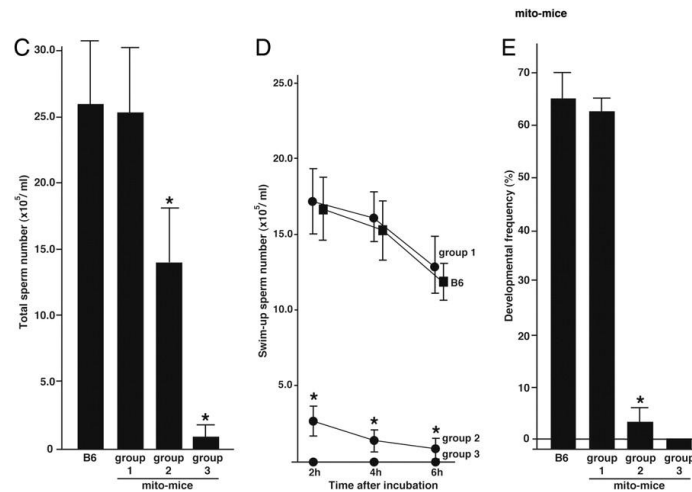
C



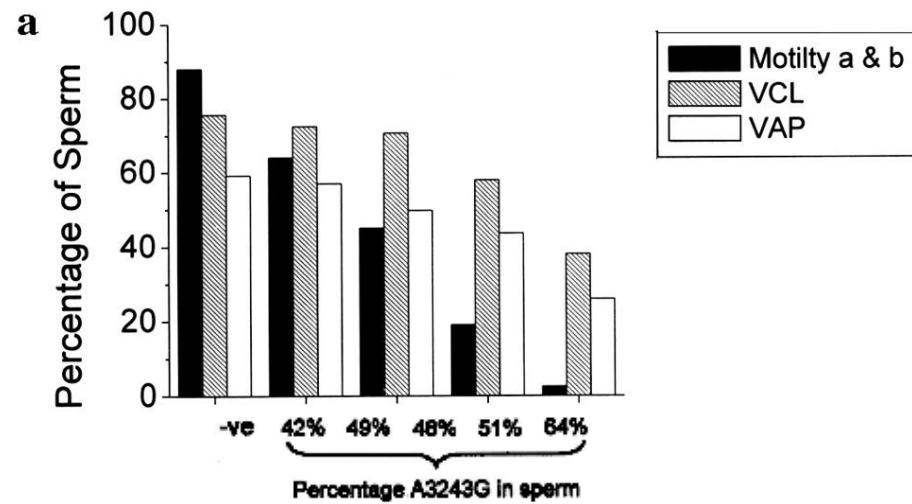
Les mâles « Mito-mice » sont infertiles

Groupe	Δ mtDNA (%)	Anomalies OXPHOS	Phénotype
1	< 68	-	normal
2	68 -75	+	intermédiaire
3	> 75	+++	Maladies mitochondriales

Δ mtDNA 4696 bp

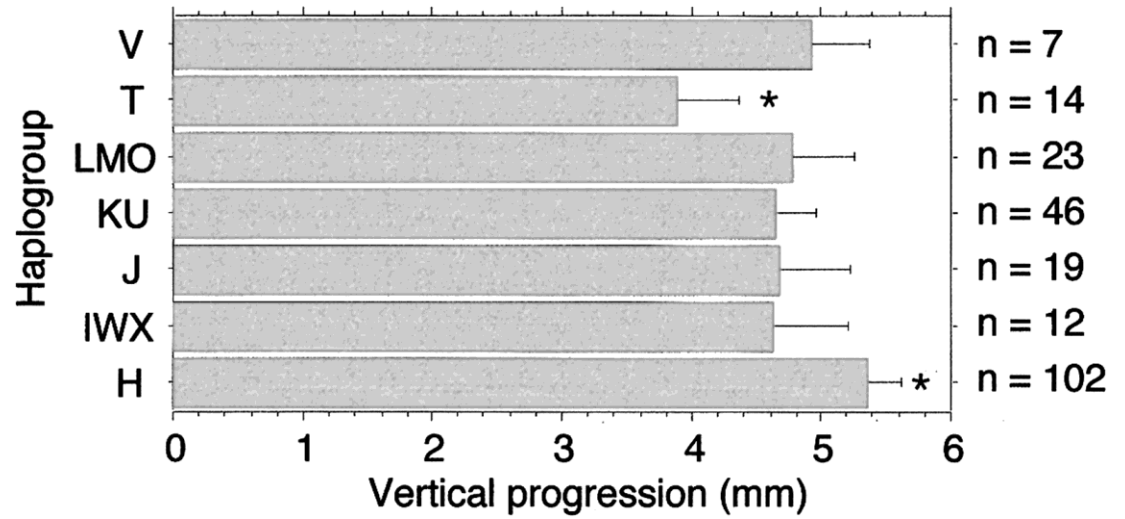
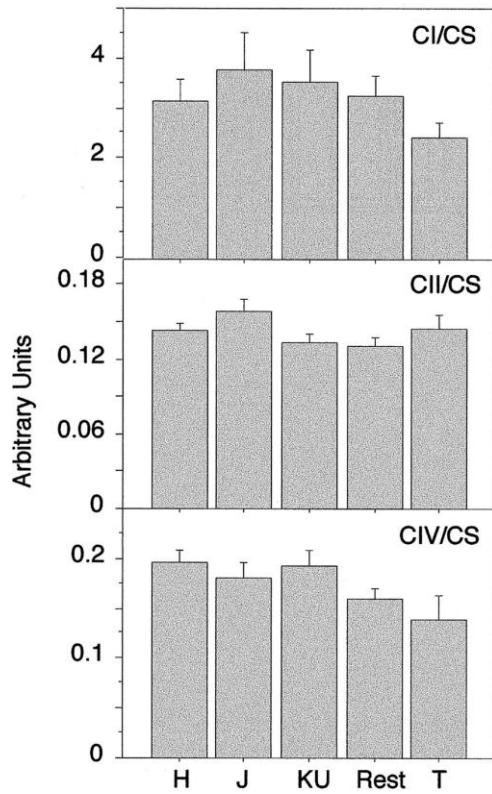


Mitochondriopathies et infertilité

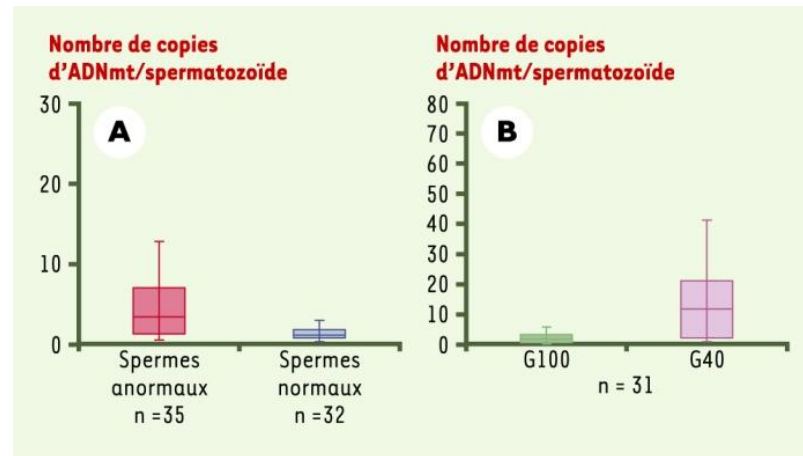


Spiropoulos, J. et al. Mol. Hum. Reprod. 2002 8:719-721

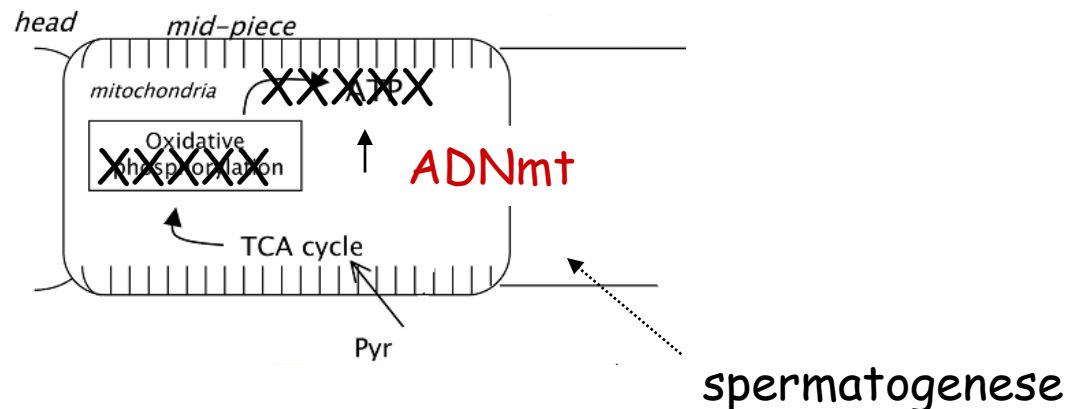
Anomalies qualitatives ADNmt et infertilité



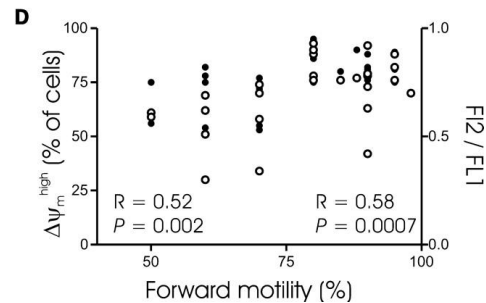
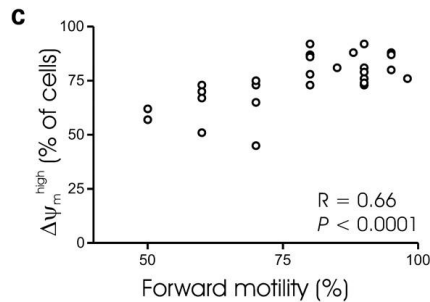
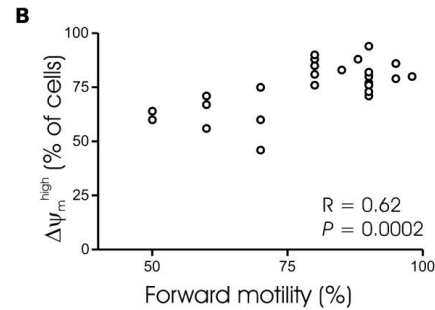
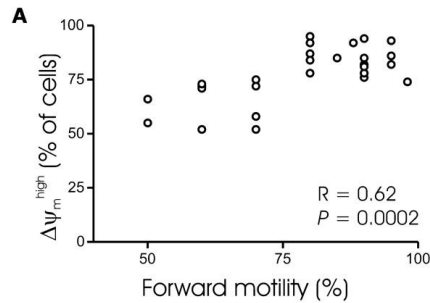
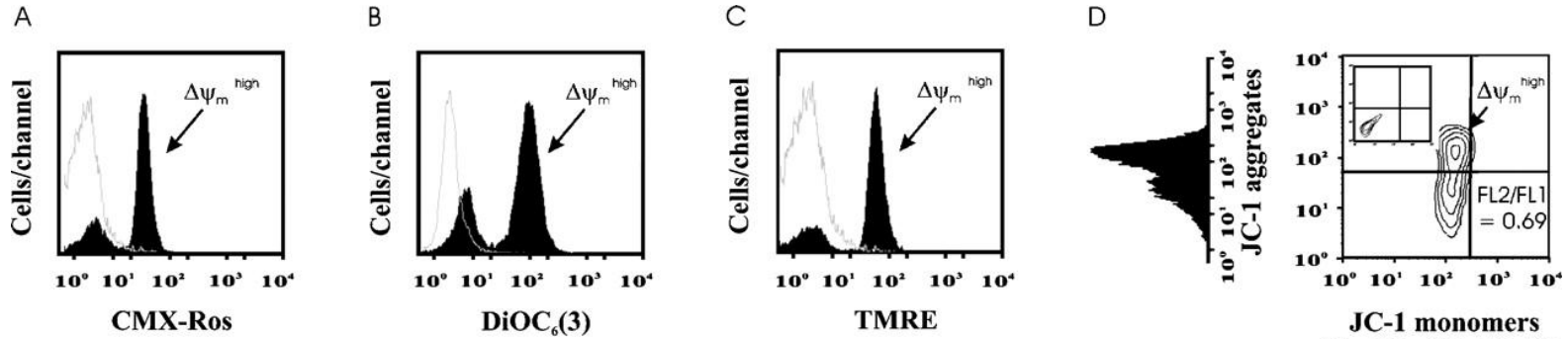
Anomalies quantitatives ADNmt et infertilité

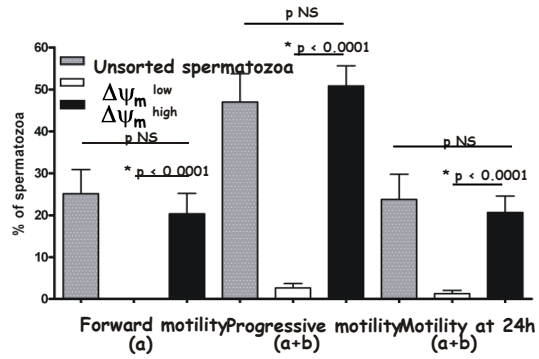
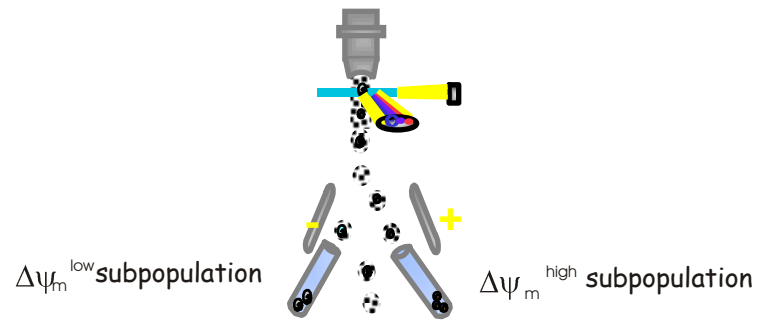
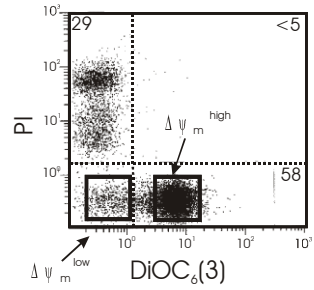


May-Panloup et al. médecine sciences, vol. 20, n° 8-9, 2004, p. 779-783



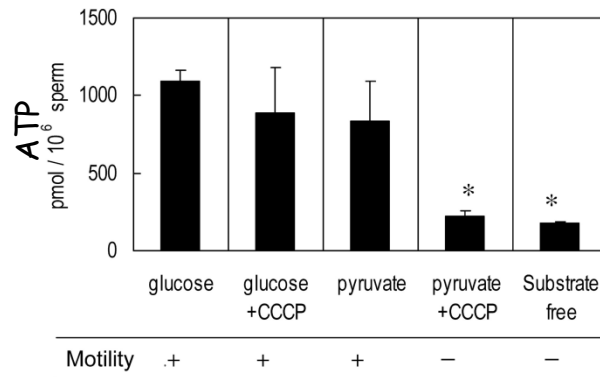
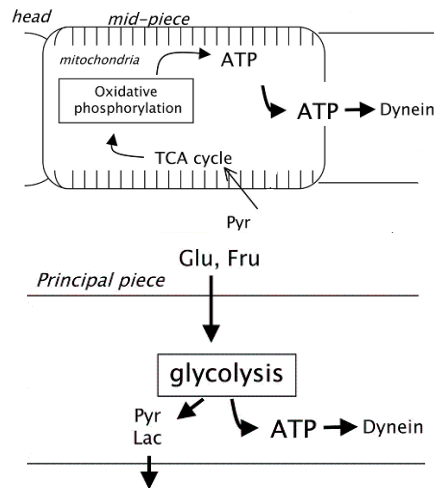
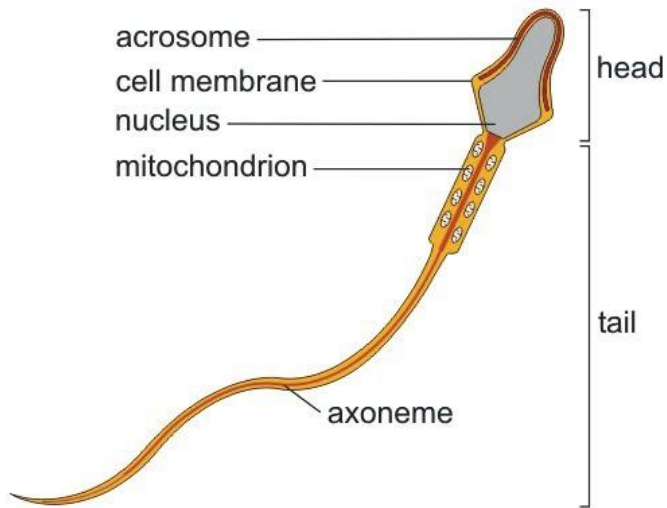
Les patients infertiles présentent-ils des anomalies mitochondriales ?





Gallon et al. Fertil Steril. 2006

mobilité des spermatozoïdes et Glycolyse ?

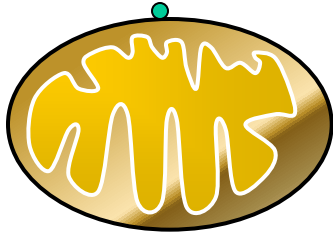


Mukai C , Okuno M Biol Reprod 2004;71:540-547

En fonction des substrats disponibles, spermatozoïde utilise glycolyse ou OXPHOS

Fonctions mitochondriales nécessaires pour la spermatogénèse ?

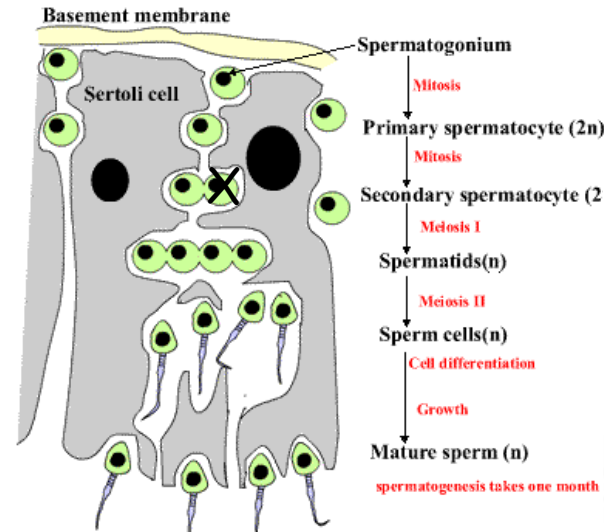
Apoptose



Fonction énergétique

Pro/anti
Bcl-2

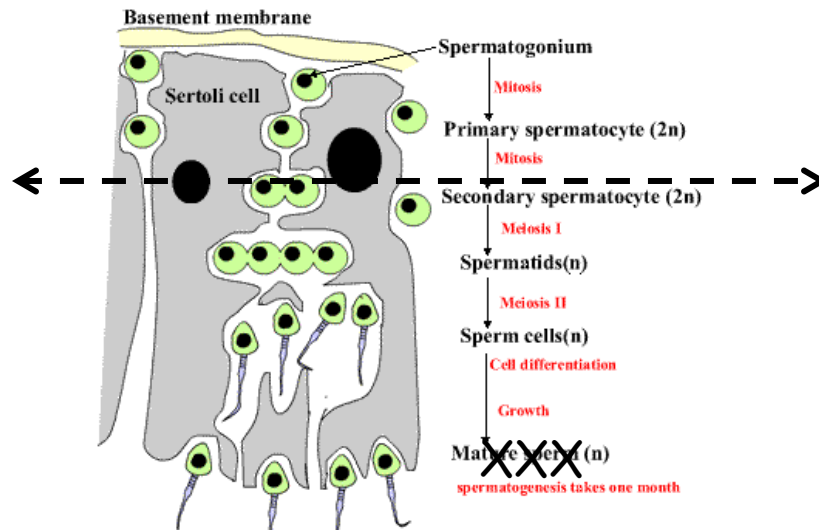
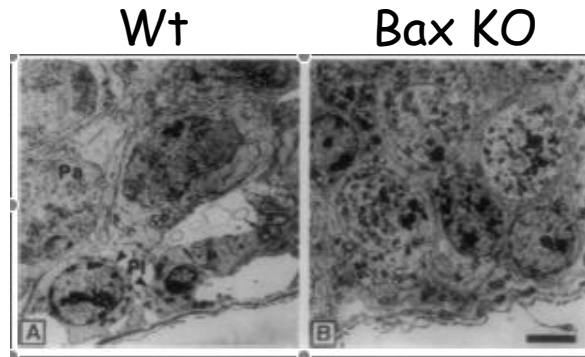
?



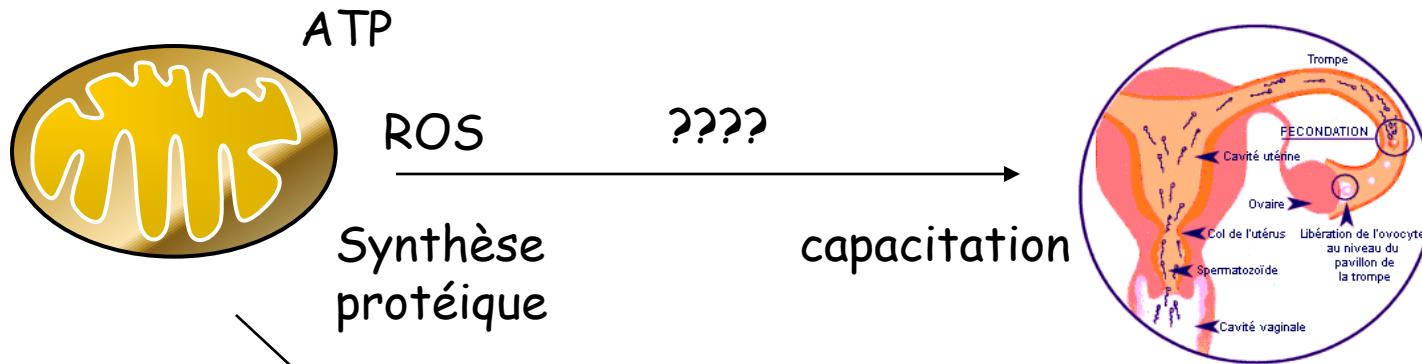
Mitose

Apoptose

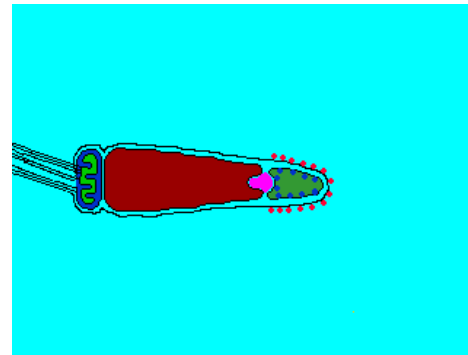
La protéine mitochondriale pro-apoptotique Bax est nécessaire à la spermatogenèse



Les souris mâles BAX KO sont infertiles



Ca²⁺ ????



R action acrosomique

Signification des altérations mitochondriales responsables de l'infertilité ?

- ROS > mutations sporadiques ADN mt
- Haplogroupes
- Toxiques : paraben, phtalate....
- Troubles de la spermatogenèse :
 - Blocage maturation

Conclusion

- Des anomalies mitochondriales (ne se résument probablement pas « énergie et mobilité ») jouent un rôle à différents stades de la reproduction
- Des anomalies mitochondriales sont retrouvées chez patients infertiles
- Intérêt de mesurer paramètres mitochondriaux fonctionnels pour BDR

Le $\Delta\Psi_m$ du spermatozoïde humain : critère prédictif discriminant de la **qualité** et du pouvoir fécondant du spermatozoïde