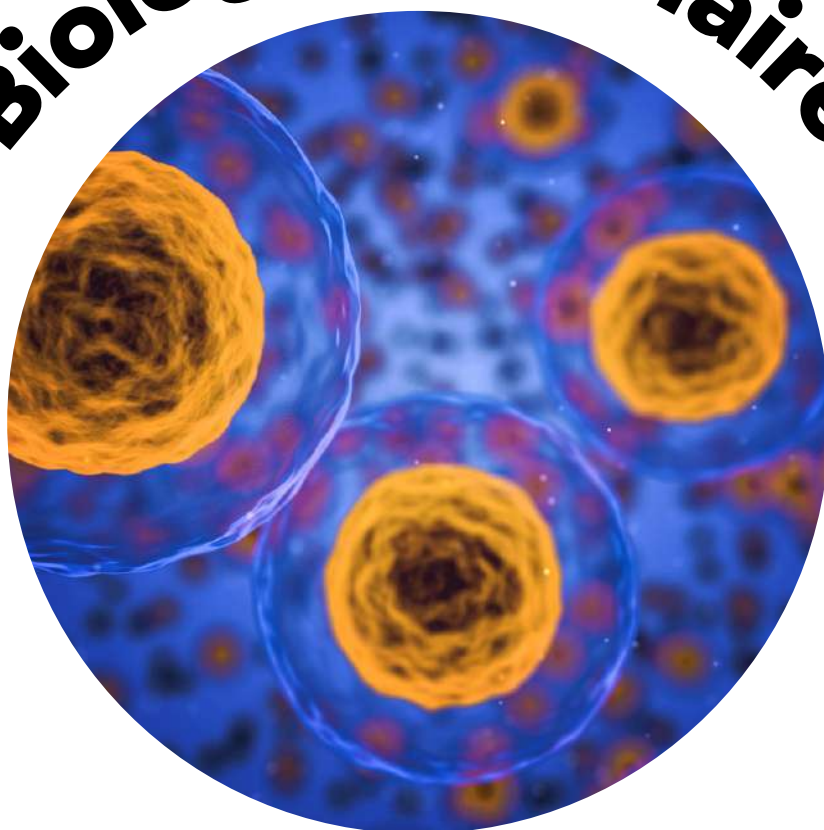


Biologie Cellulaire



SCIENCES DE LA
VIE ET DE LA TERRE



Shop



- Cahiers de Biologie + Lexique
- Accessoires de Biologie



Etudier



Visiter [Biologie Maroc](http://www.biologie-maroc.com) pour étudier et passer des QUIZ et QCM en ligne et Télécharger TD, TP et Examens résolus.



Emploi



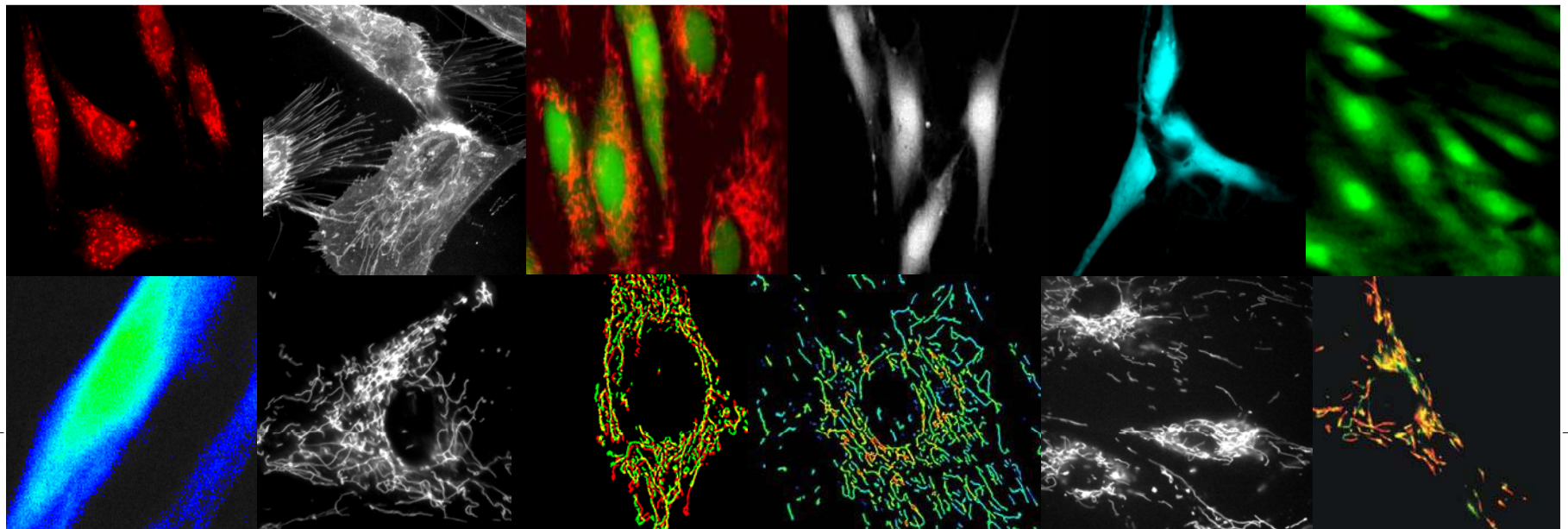
- CV • Lettres de motivation • Demandes...
- Offres d'emploi
- Offres de stage & PFE



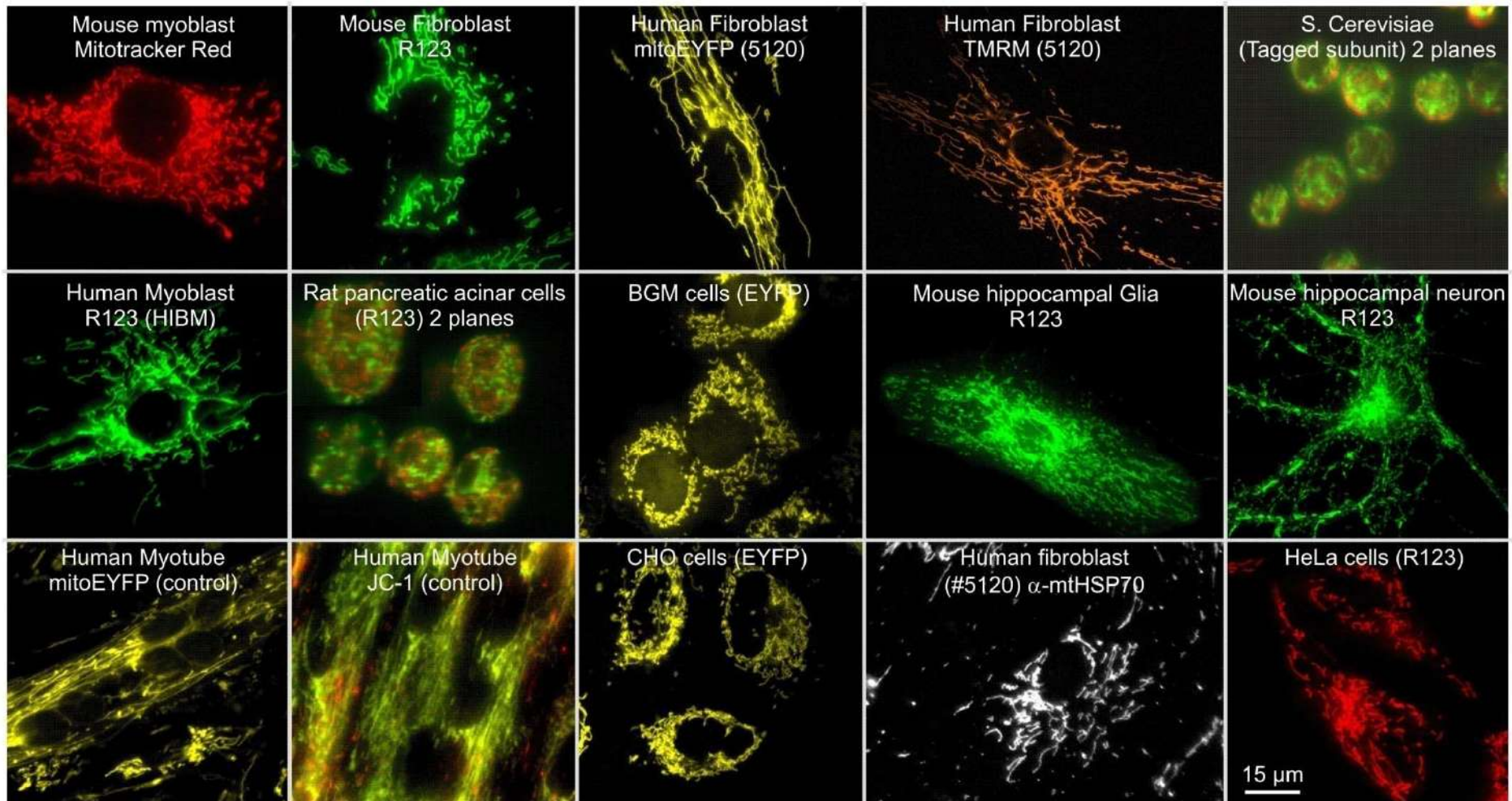
Mitochondrial structure-function relationships

Werner J.H. Koopman, PhD.

Dept. of Membrane Biochemistry NCMLS
Radboud University Nijmegen Medical Centre
Nijmegen, The Netherlands
w.koopman@ncmls.ru.nl



Mitochondrial structure is diverse

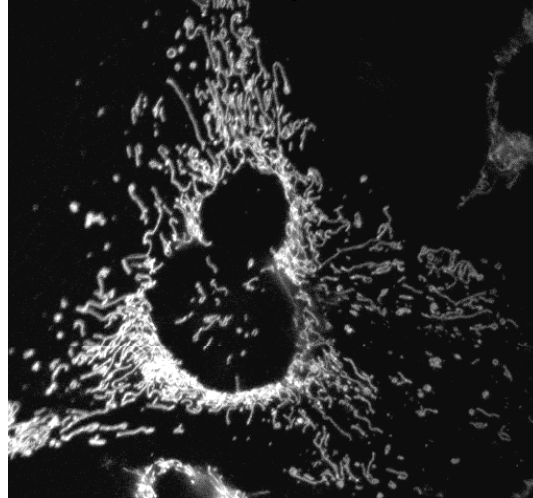


Mitochondrial structure is dynamic

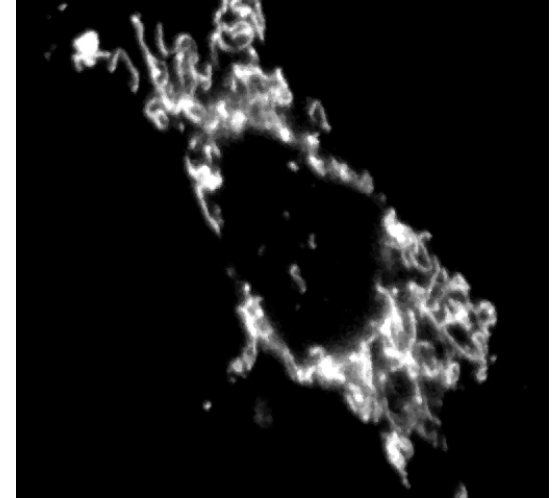
Mouse myoblasts



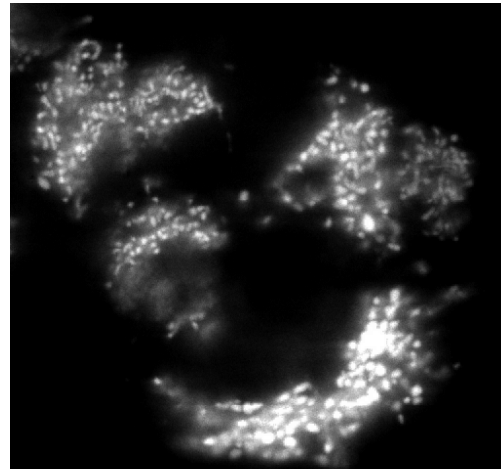
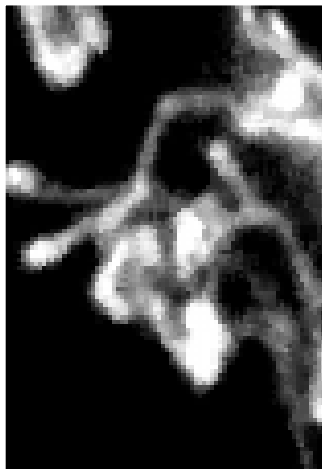
Hamster ovary fibroblasts



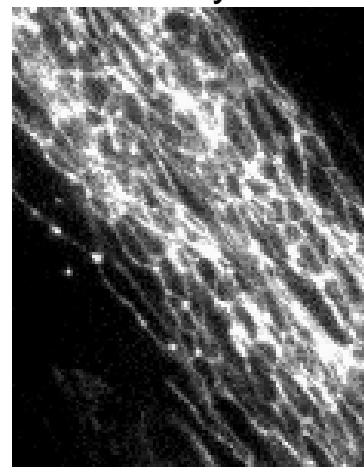
Mouse embryonic fibroblasts



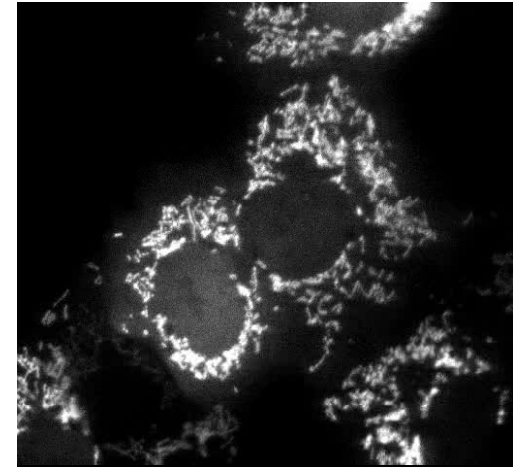
HEK293 cells



Human myotubes

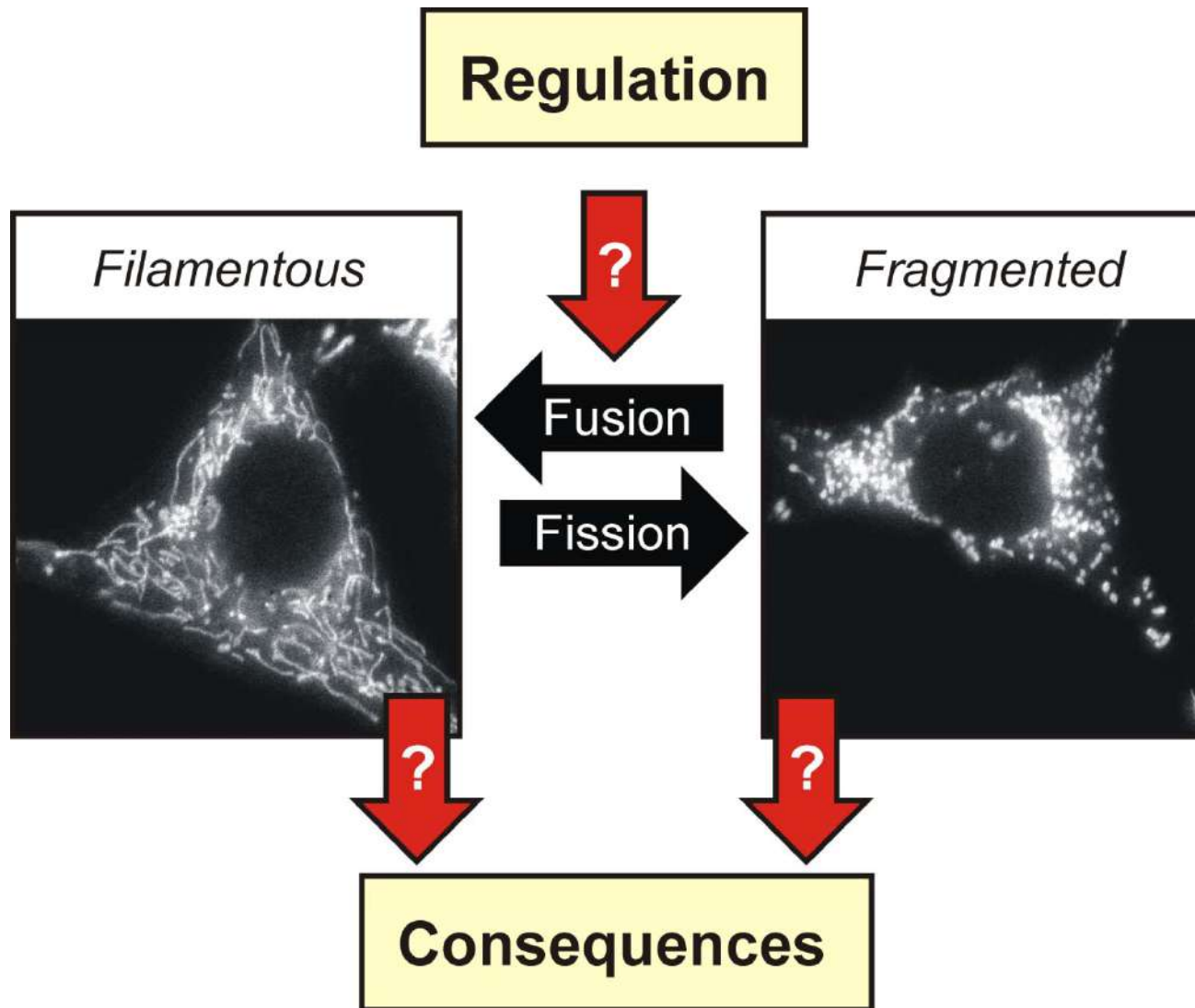


BGM cells

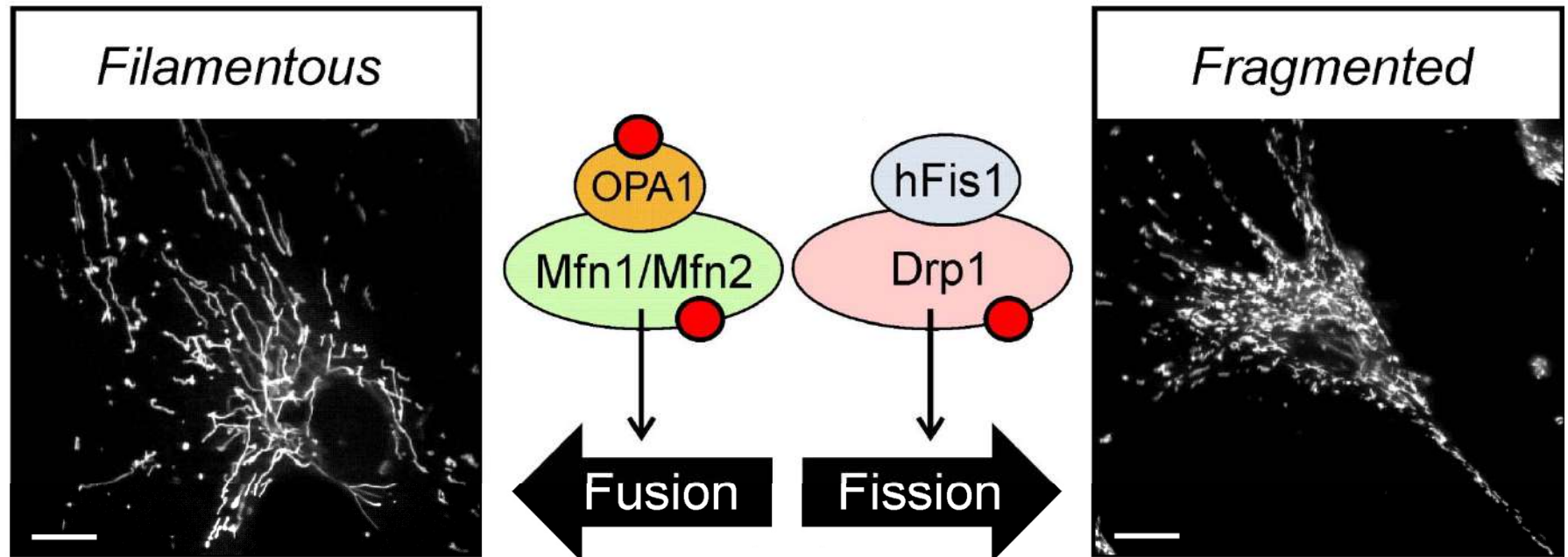


DYNAMICS: Motility – Structure – Position – Matrix

Concept of research



Mitochondrial dynamics is regulated by multifunctional fusion and fission proteins



- Apoptosis (Drp1, OPA1, hFis1, Mfn2)
- ER morphology (Mfn2)
- ER mitochondria communication (Mfn2)
- Peroxisome fission (hFis1, Drp1)
- OXPHOS expression (Mfn2)



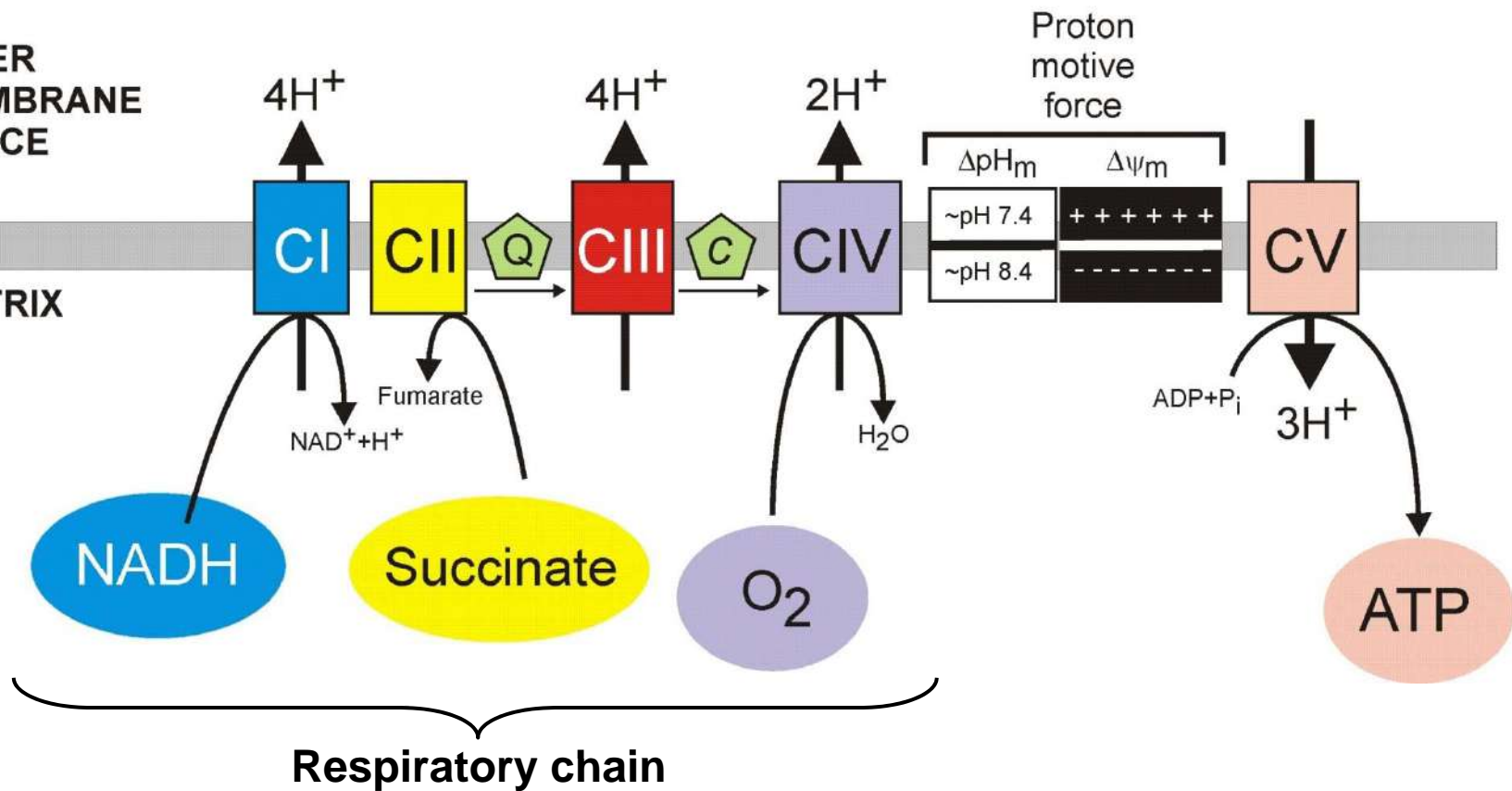
- Cell survival
- Ca²⁺ and ATP handling
- Metabolism

Mitochondrial and cellular metabolism is sustained by the respiratory chain

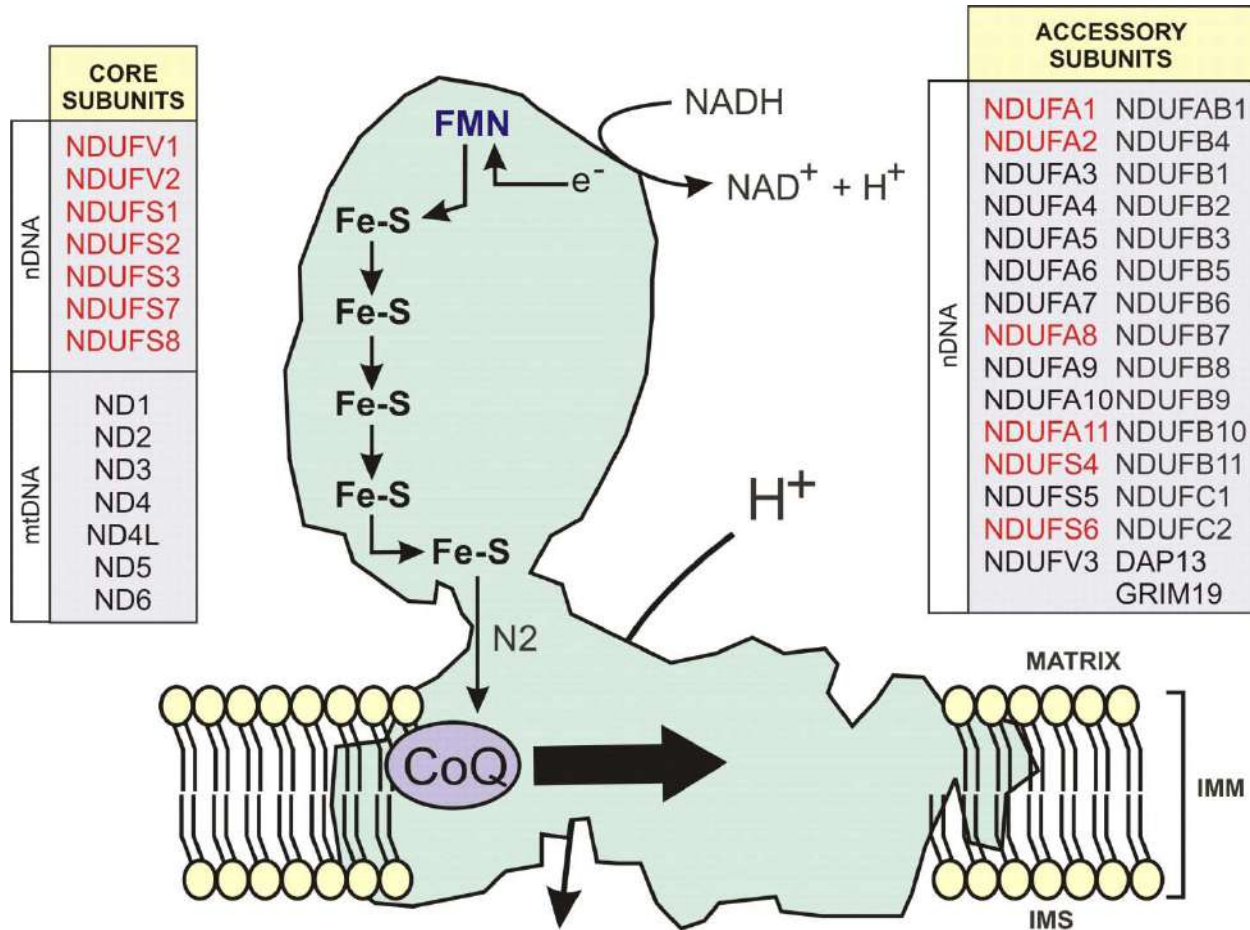
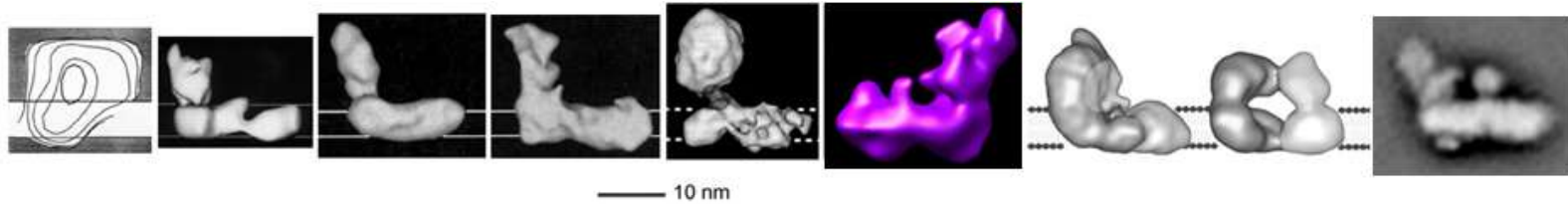
CYTOSOL

INTER MEMBRANE SPACE

MATRIX

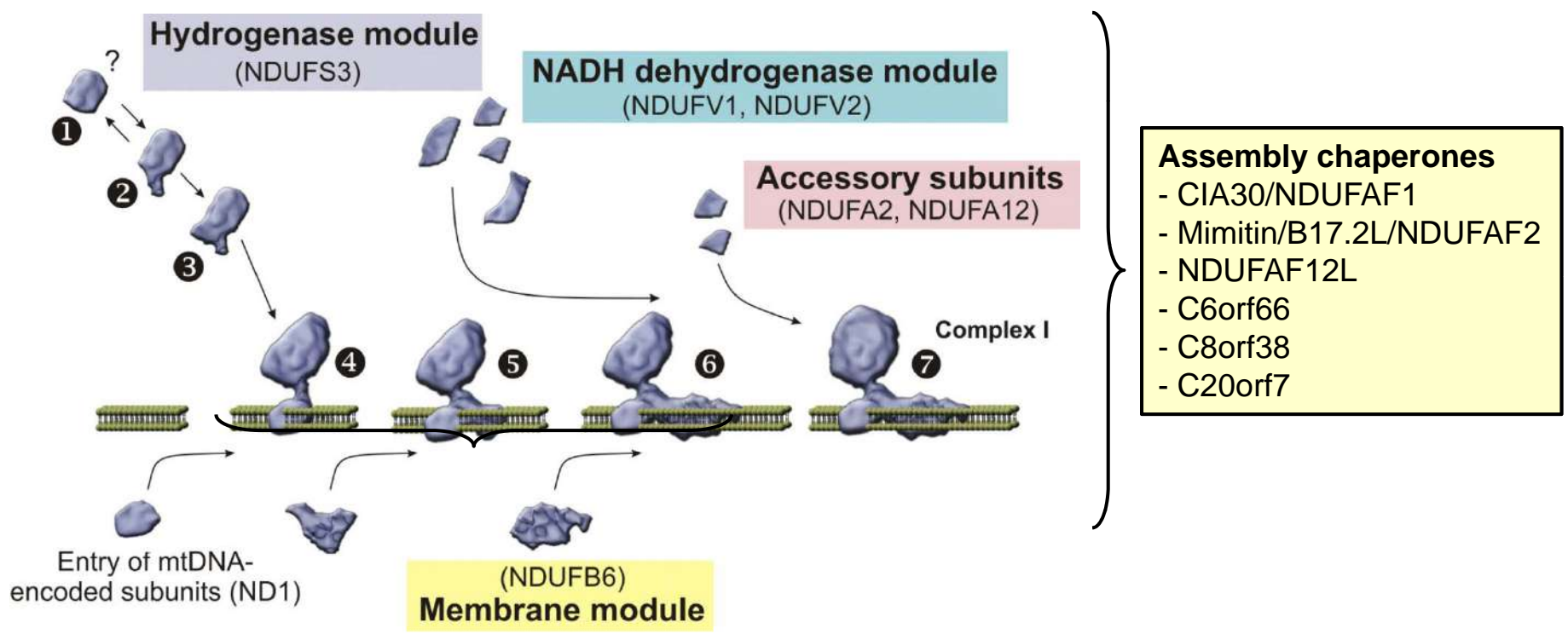
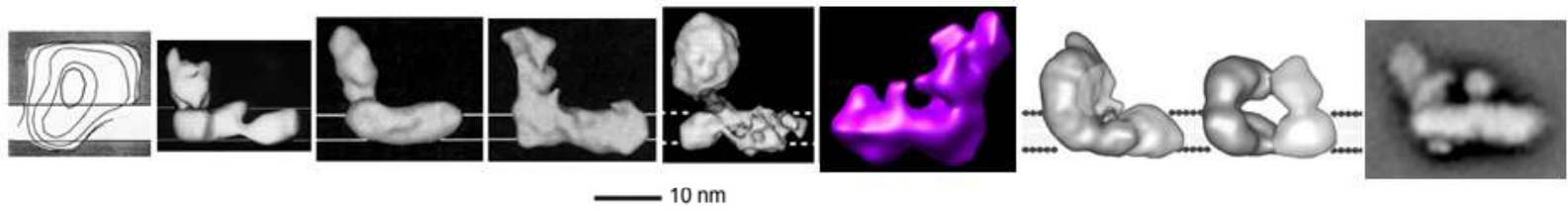


Complex I : structure and function

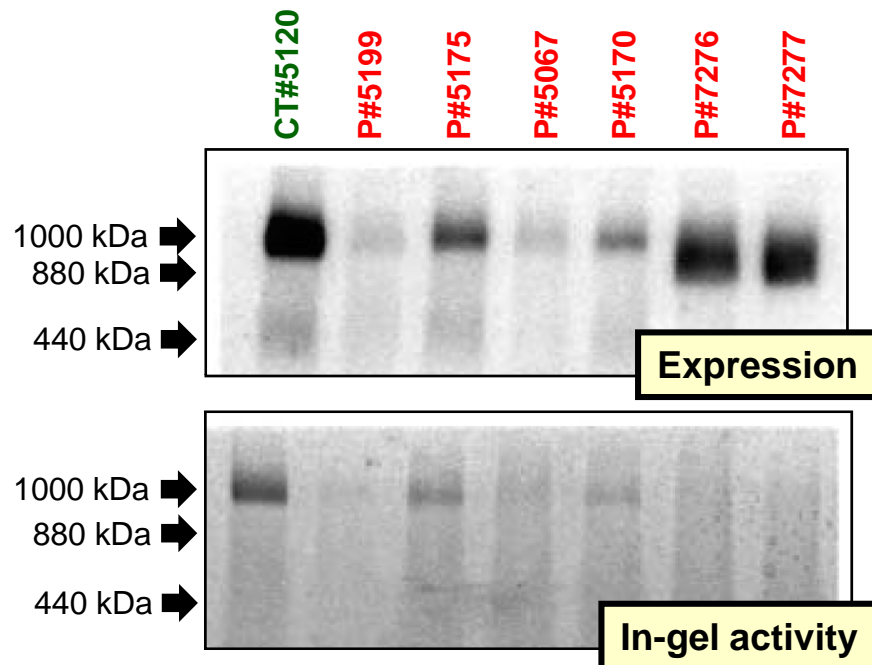




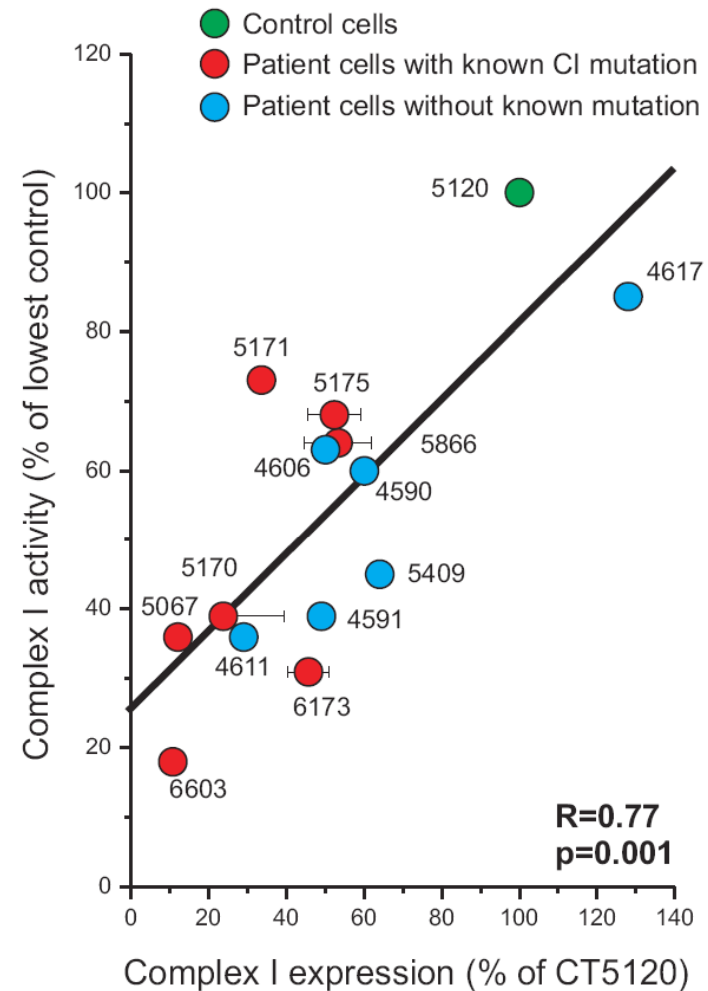
Complex I assembly requires multiple assembly chaperones



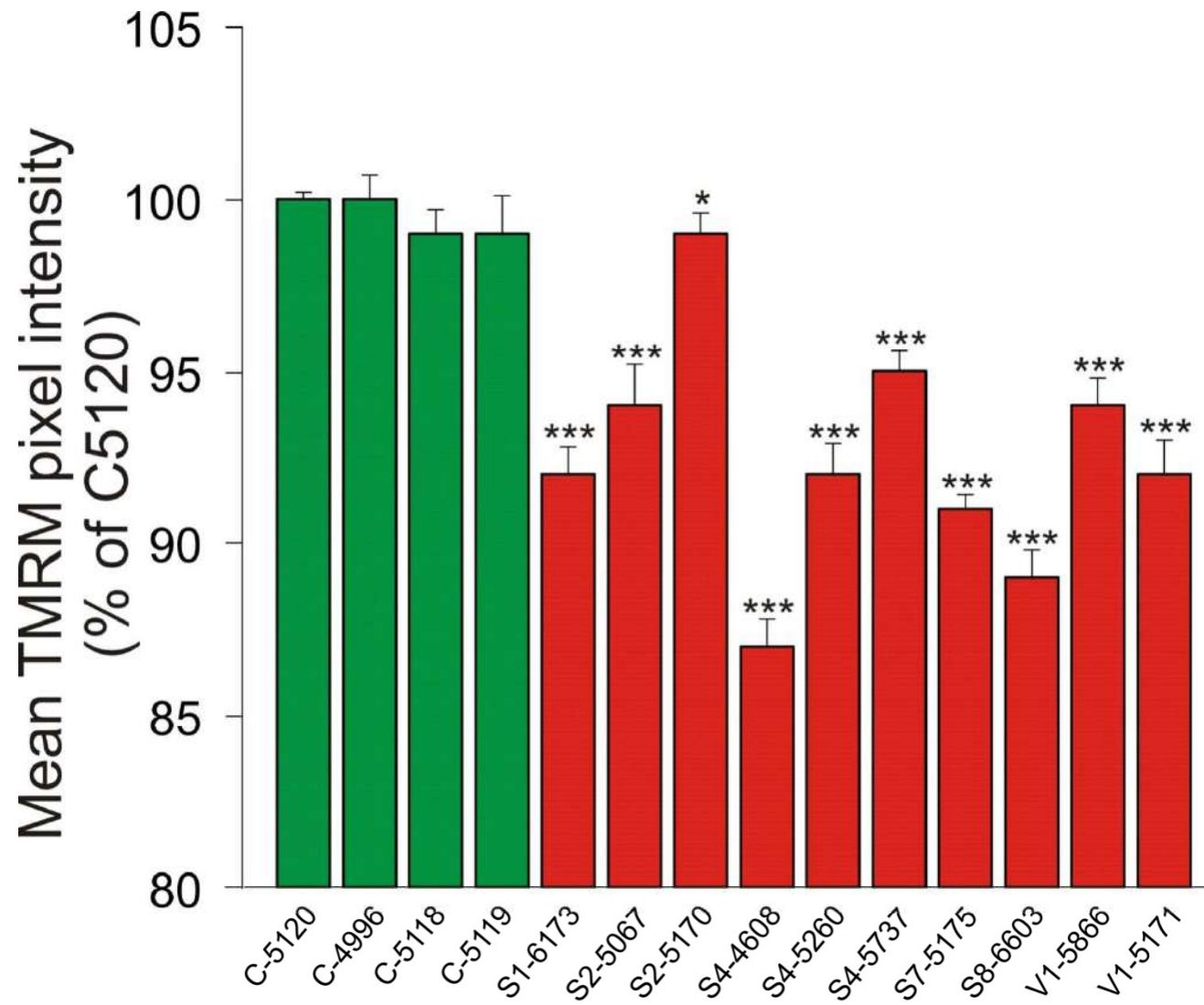
Complex I expression and activity: reduced in patient fibroblasts



SO: Mutations reduce
The expression/activity
of fully-assembled
complex I

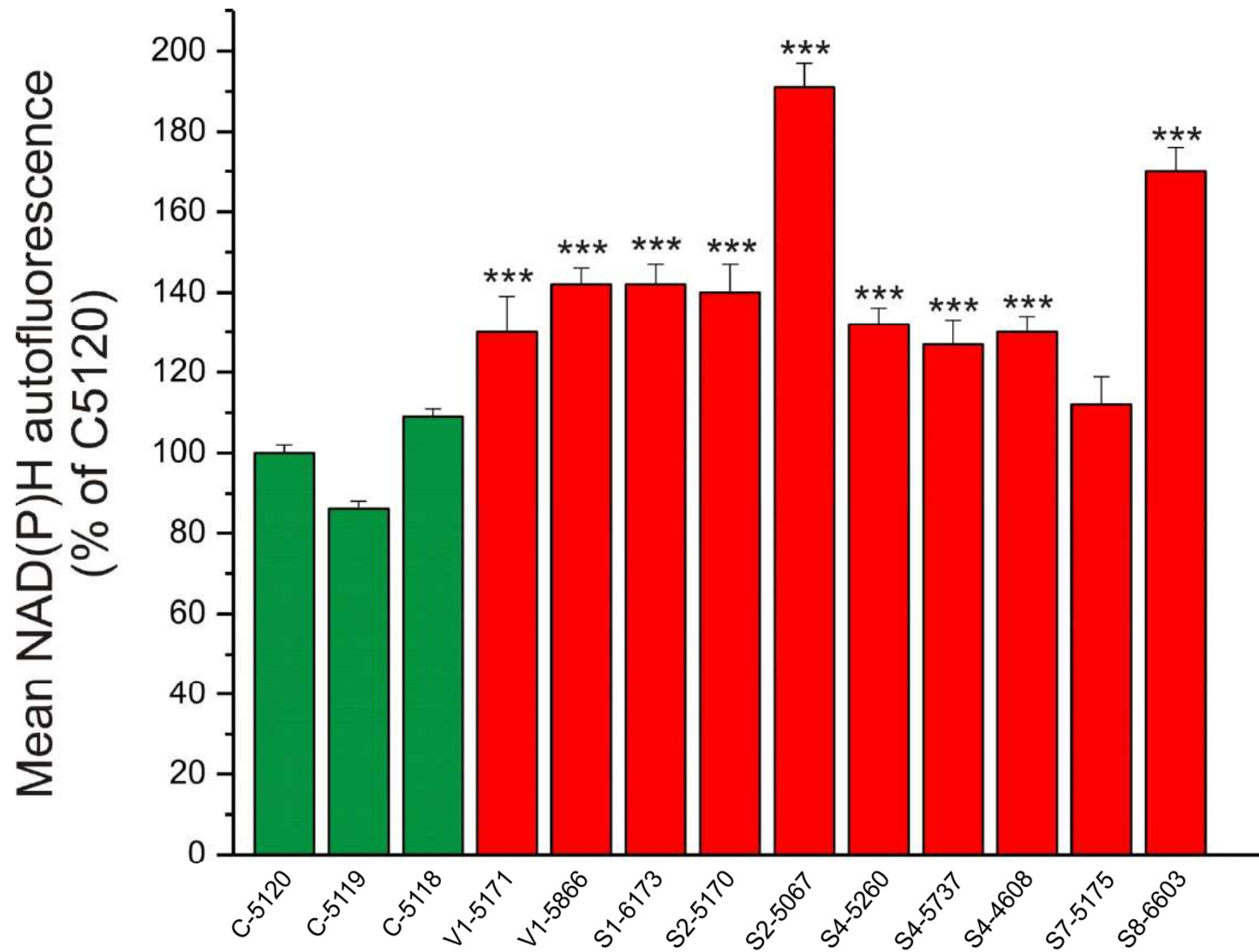


Human complex I deficiency: $\Delta\psi$ is depolarized

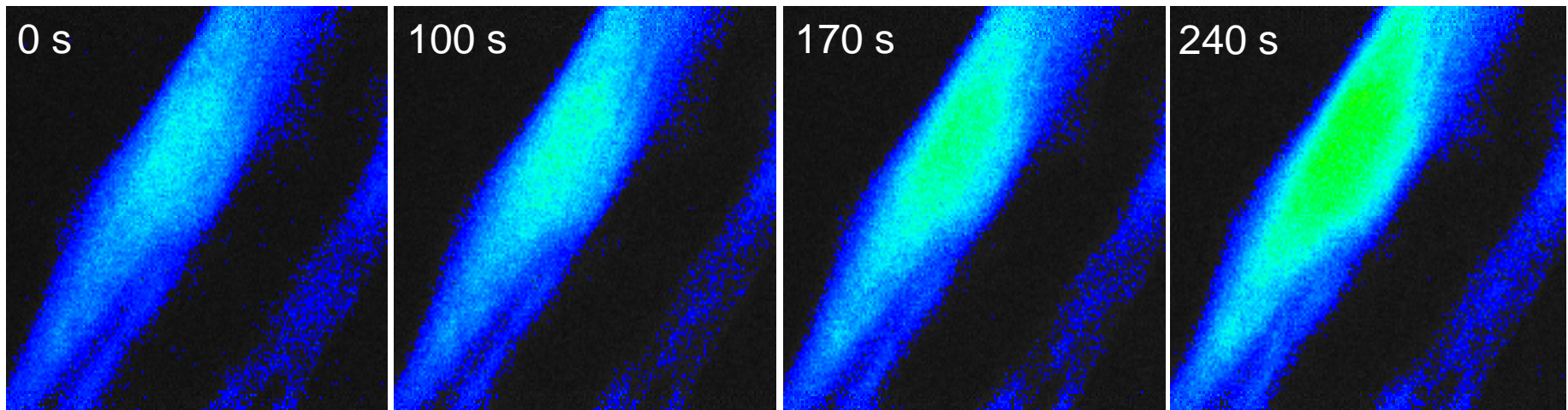
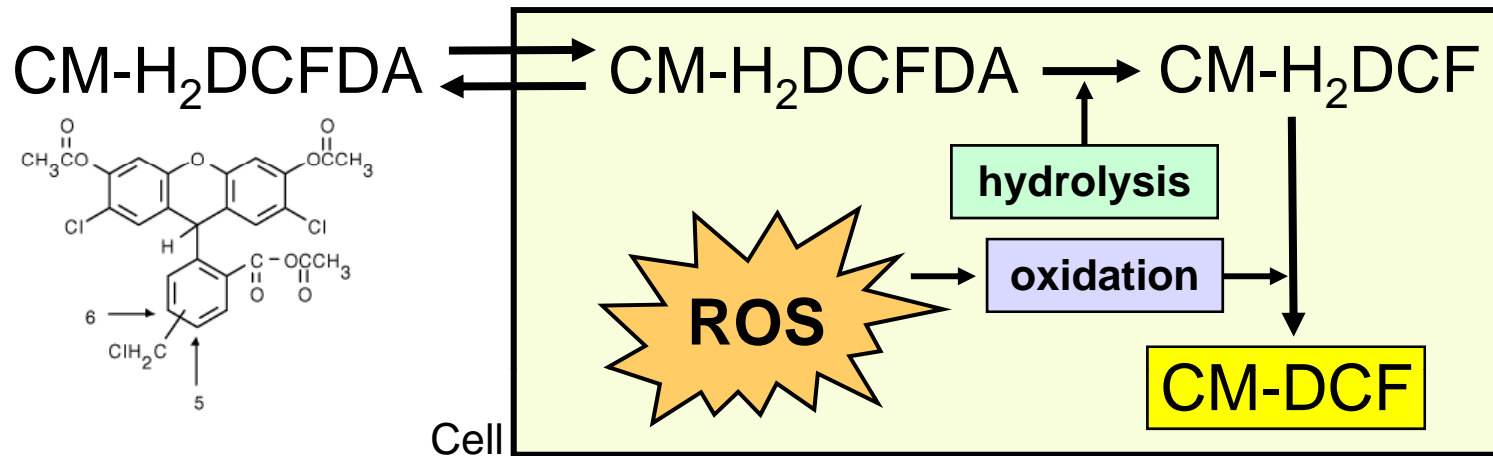




Human complex I deficiency: NAD(P)H levels are elevated



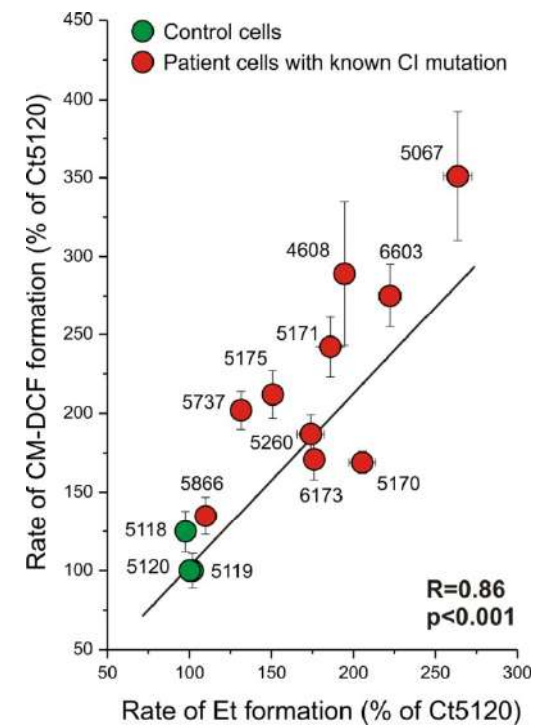
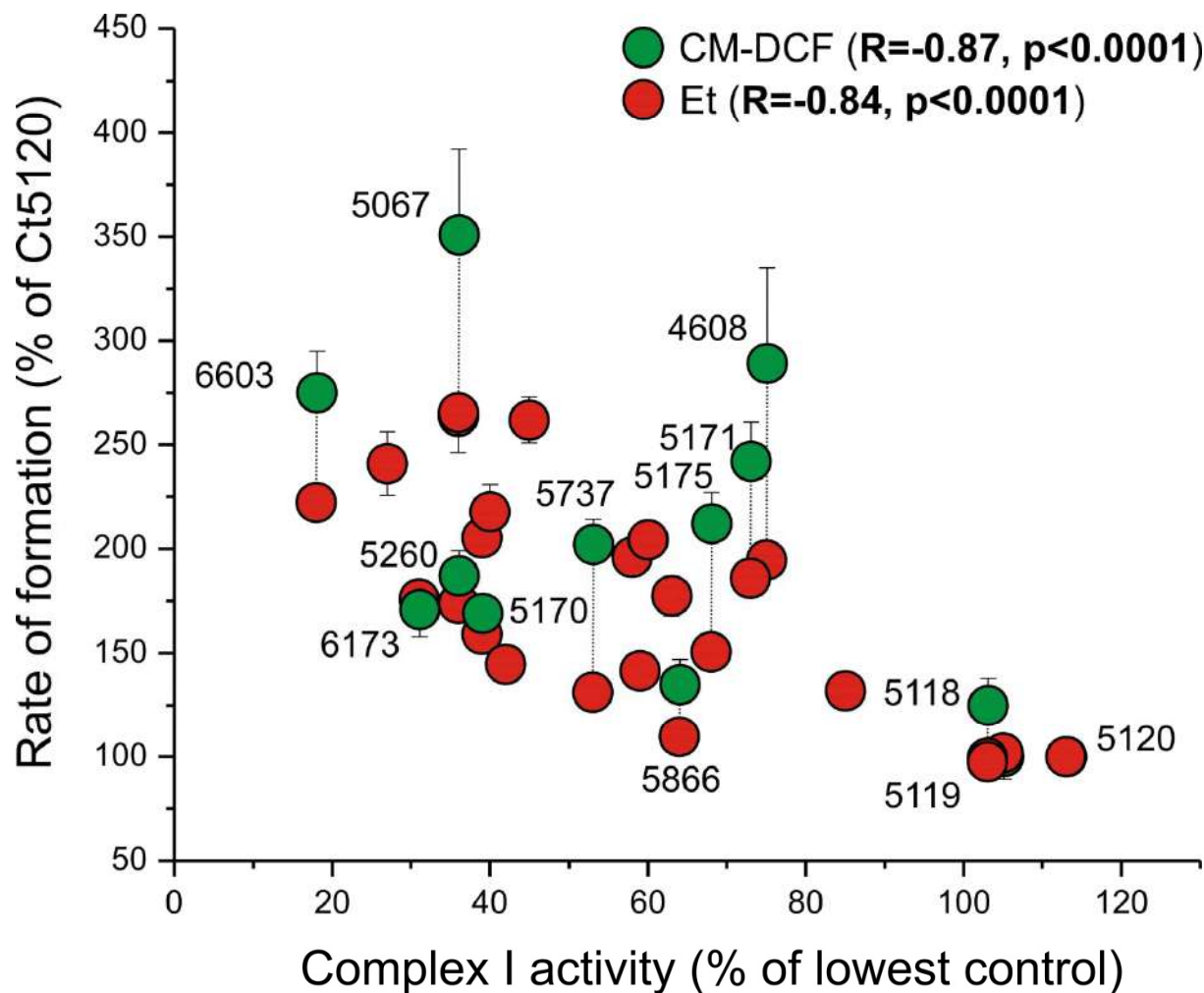
Measurement of cellular ROS using CM-H₂DCFDA



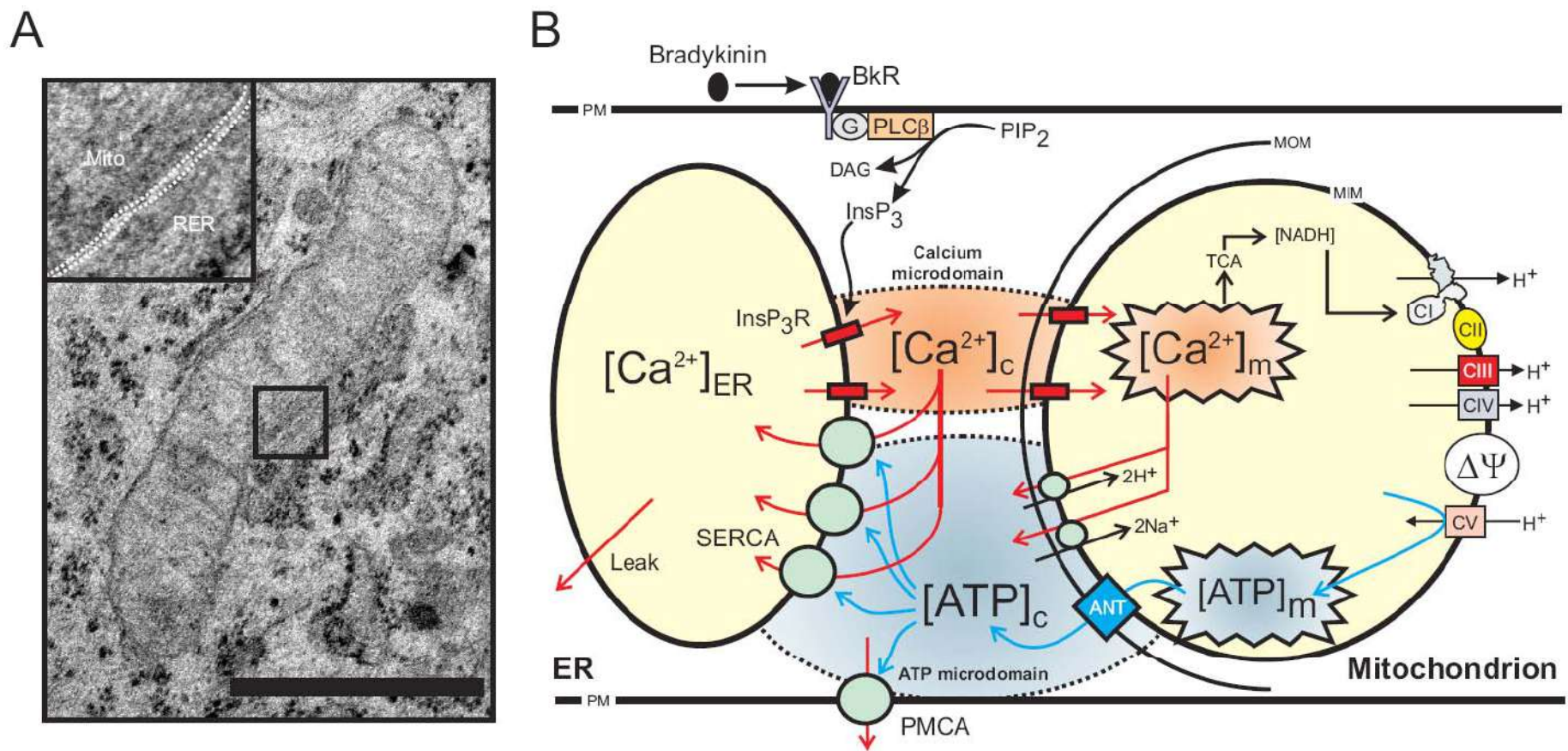
15 μ m



Human complex I deficiency: Reactive oxygen species levels are elevated

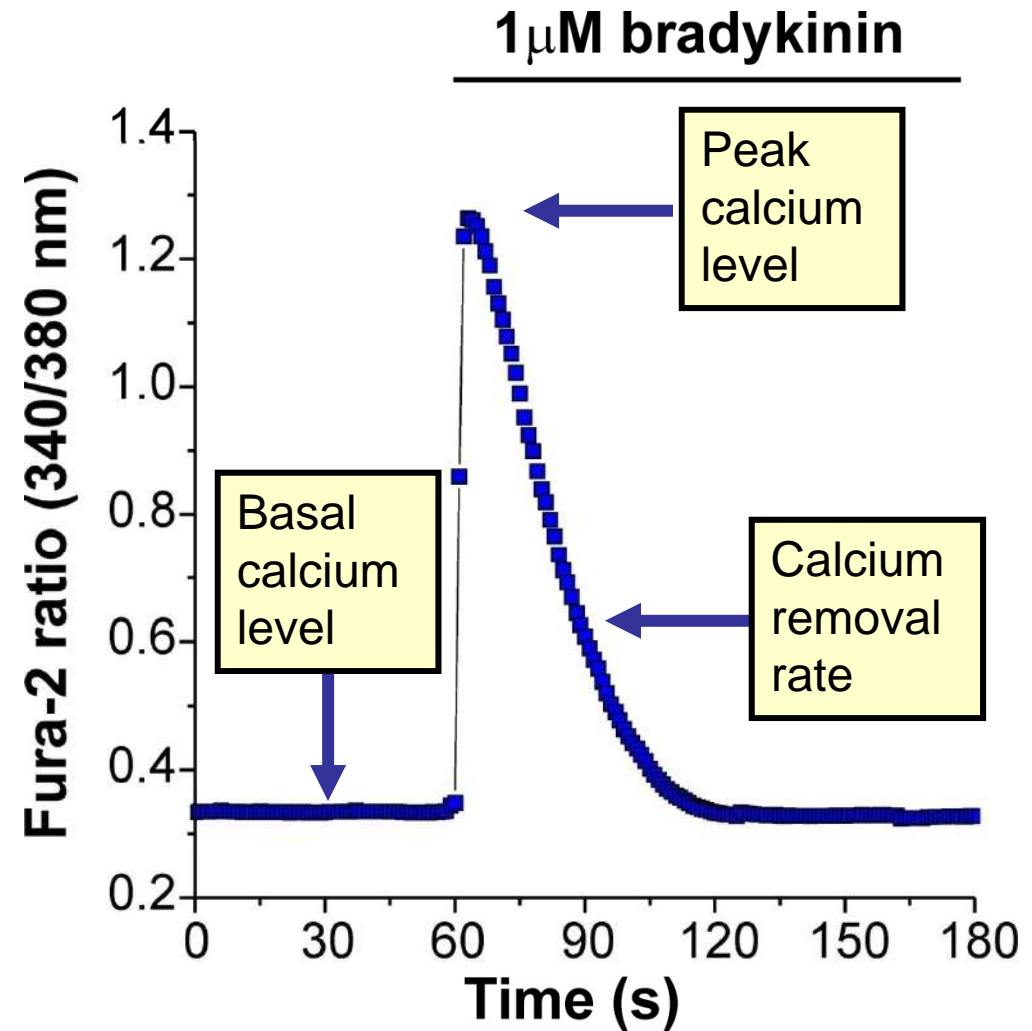
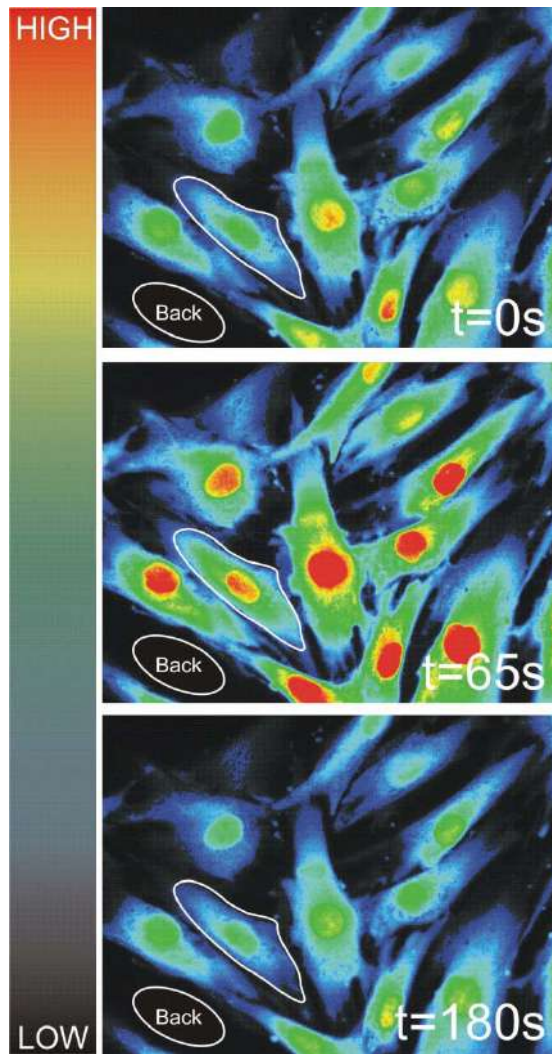


Mitochondria-ER Ca^{2+} handling

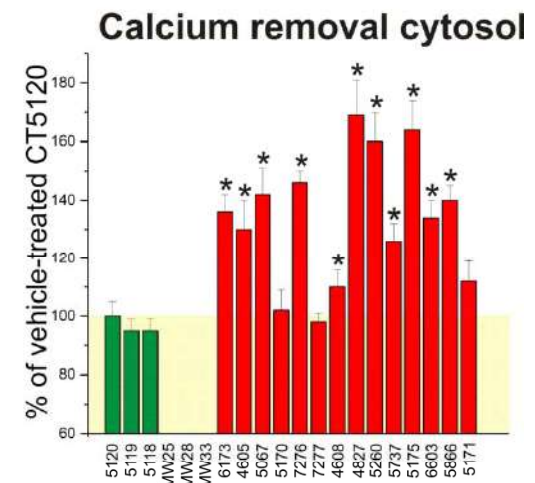
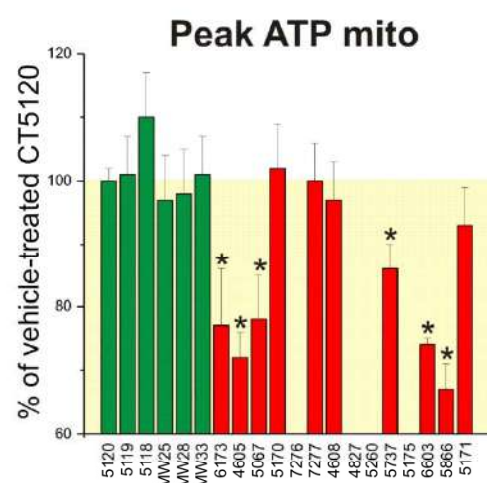
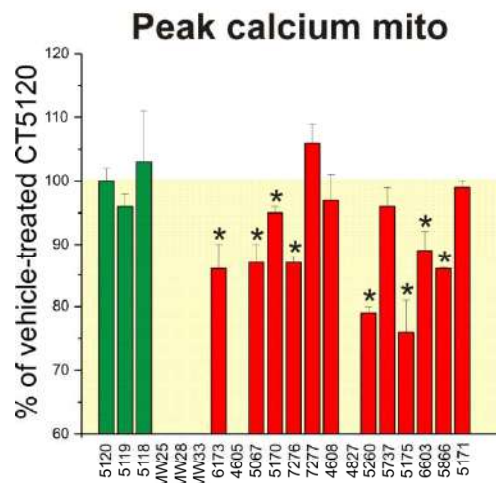
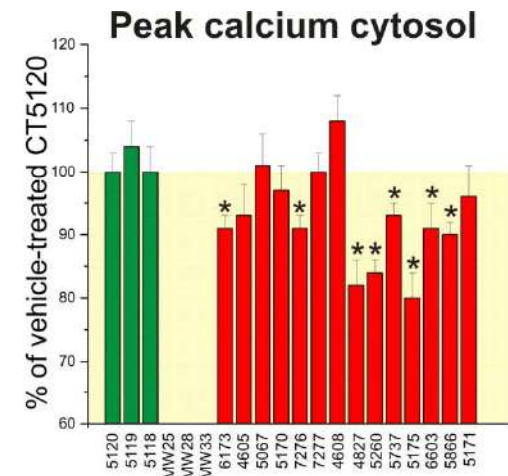
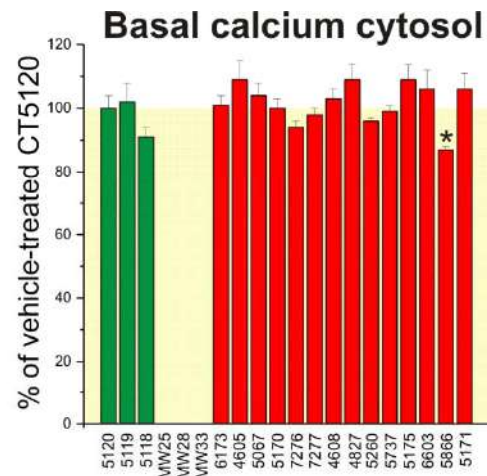
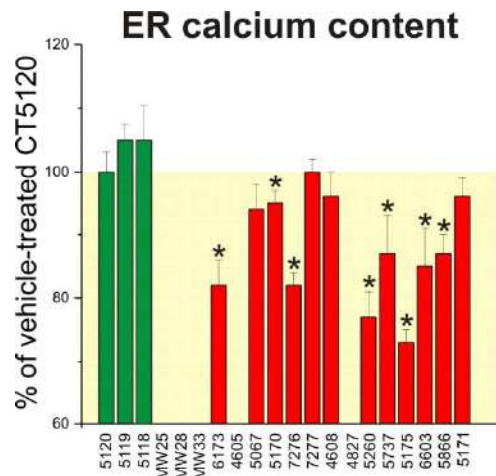


Tethers: (A) $InsP_3R \rightarrow mtHSP70 \rightarrow VDAC/Porin$
 (B) $Mfn2_{ER} \rightarrow Mfn2_{mito}$

Cytosolic calcium handling in human skin fibroblasts: Fura-2



Human complex I deficiency: Ca^{2+} and ATP handling are disturbed



Visch et al., JBC, 2004; Visch et al., BBA, 2005
 Visch et al., AJP, 2006; Willems et al., Cell Calcium, 2008
 Valsecchi et al. (Submitted)



Human complex I deficiency: Key cellular consequences



(I) Less fully-assembled and active complex I protein

(II) Depolarized mitochondrial membrane potential

(III) Increased NAD(P)H and ROS levels

(IV) Altered cellular and mitochondrial ATP/Ca²⁺ handling

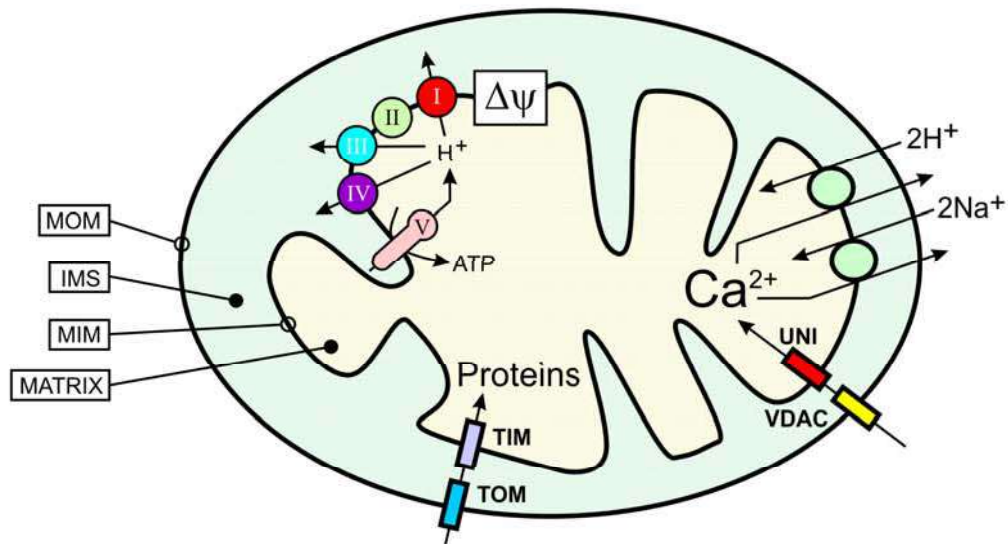


Q1: How does this relate to mitochondrial morphology?

Q2: Can complex I deficiency be mitigated?

Visualizing mitochondrial structure with fluorescent proteins and cations

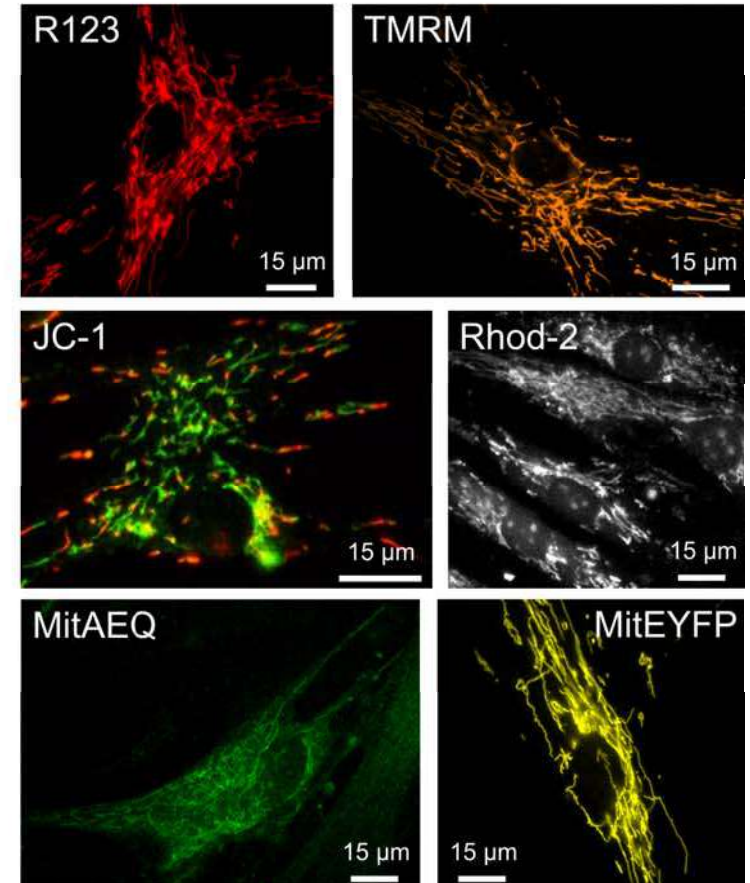
A



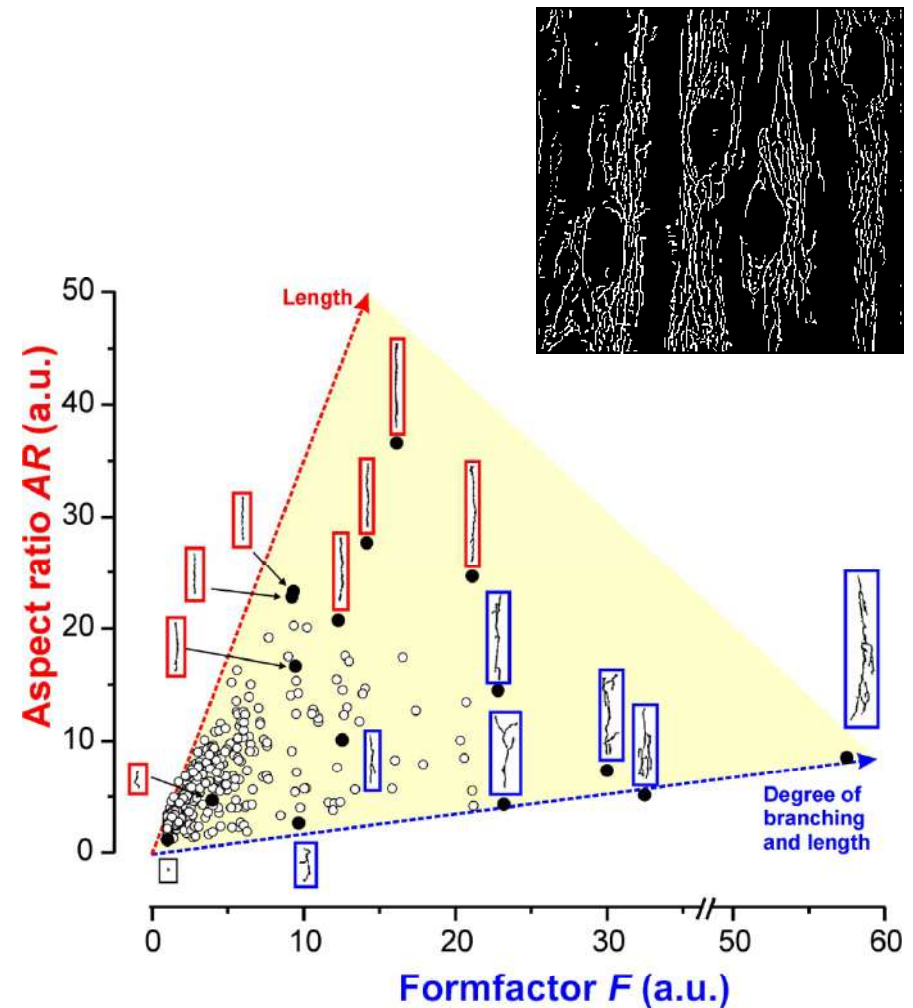
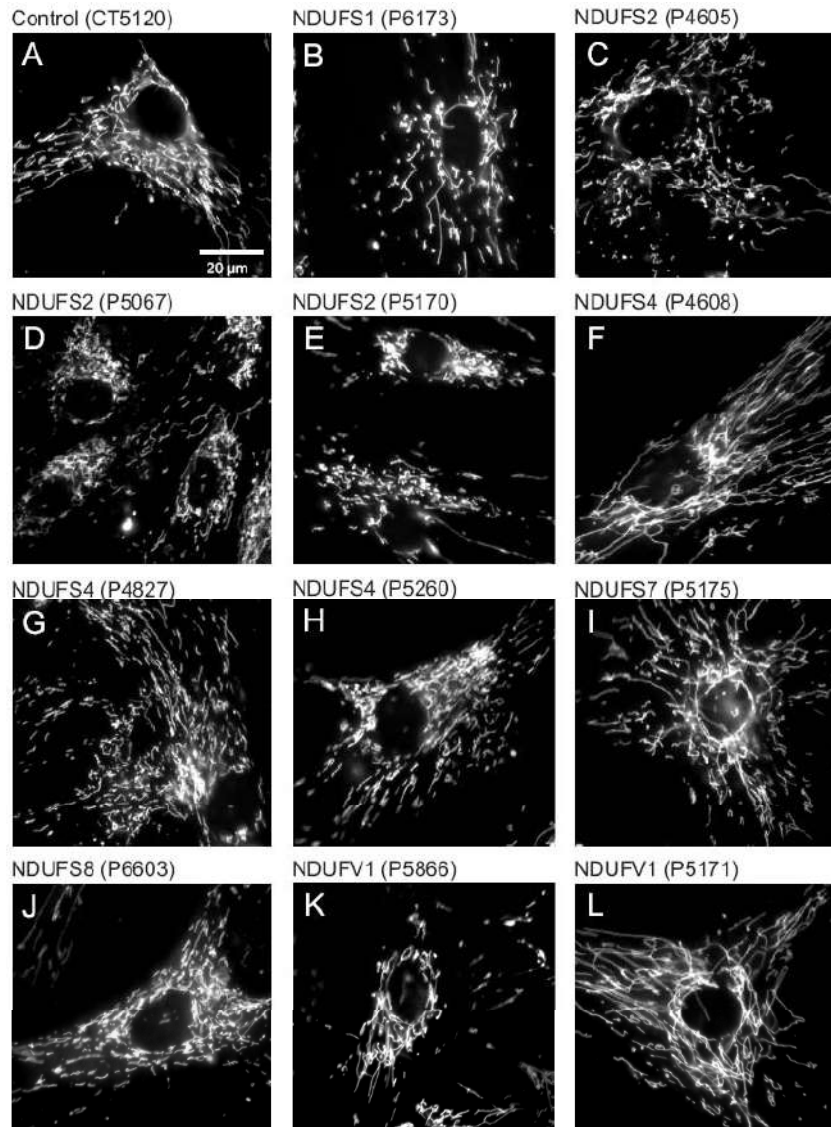
B

$$\Delta\psi \text{ (mV)} = \frac{2.303 \cdot RT}{zF} \log \frac{[\text{Cation}]_{in}}{[\text{Cation}]_{out}}$$

C



Complex I deficient patient cell lines: Different mitochondrial morphologies

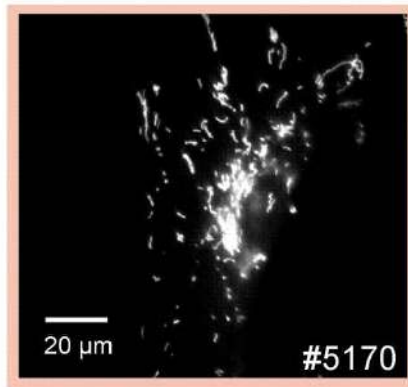




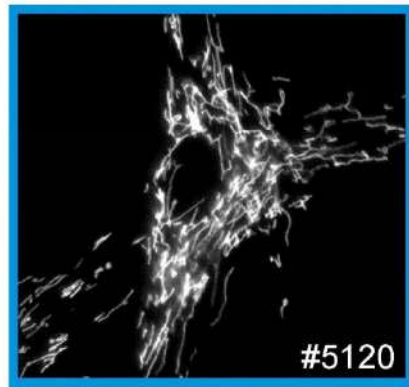
Complex I deficient patient cell lines: Two 'types' of mitochondrial morphologies



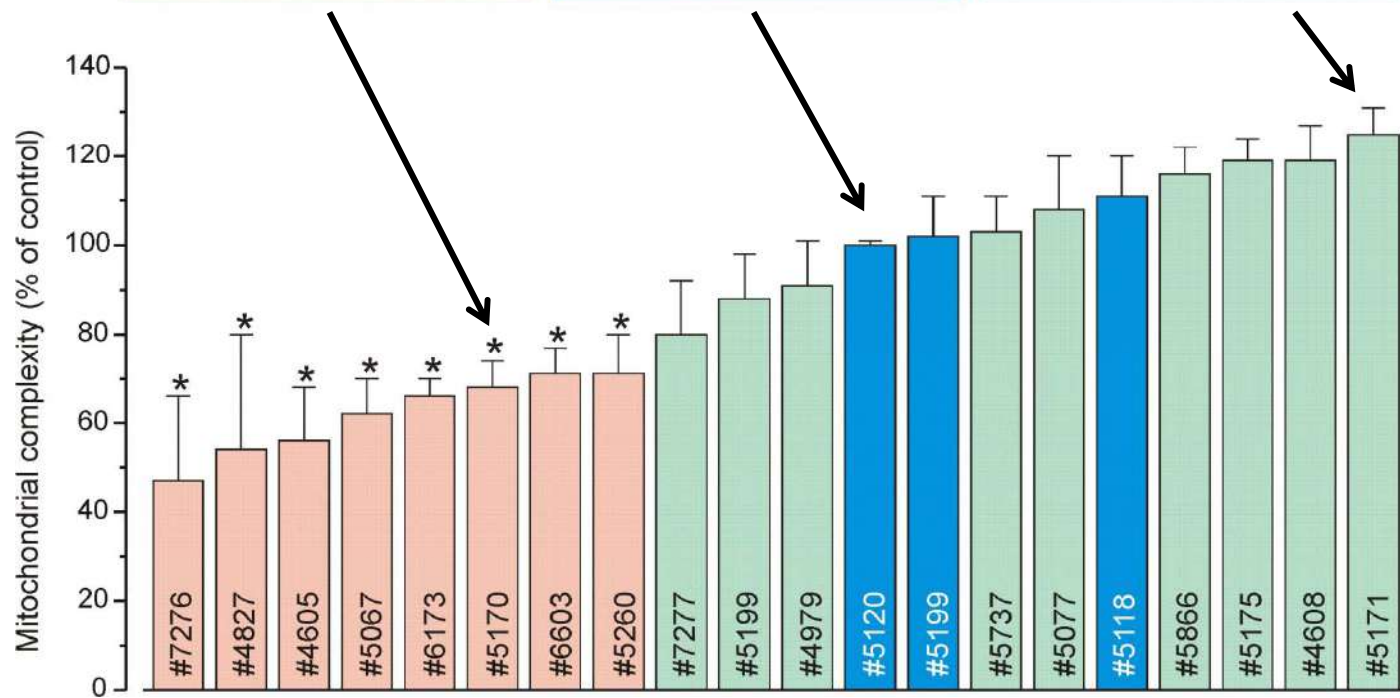
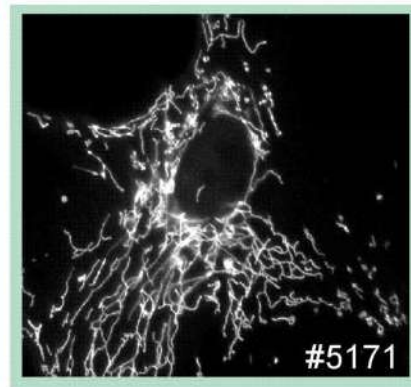
Patient: fragmented



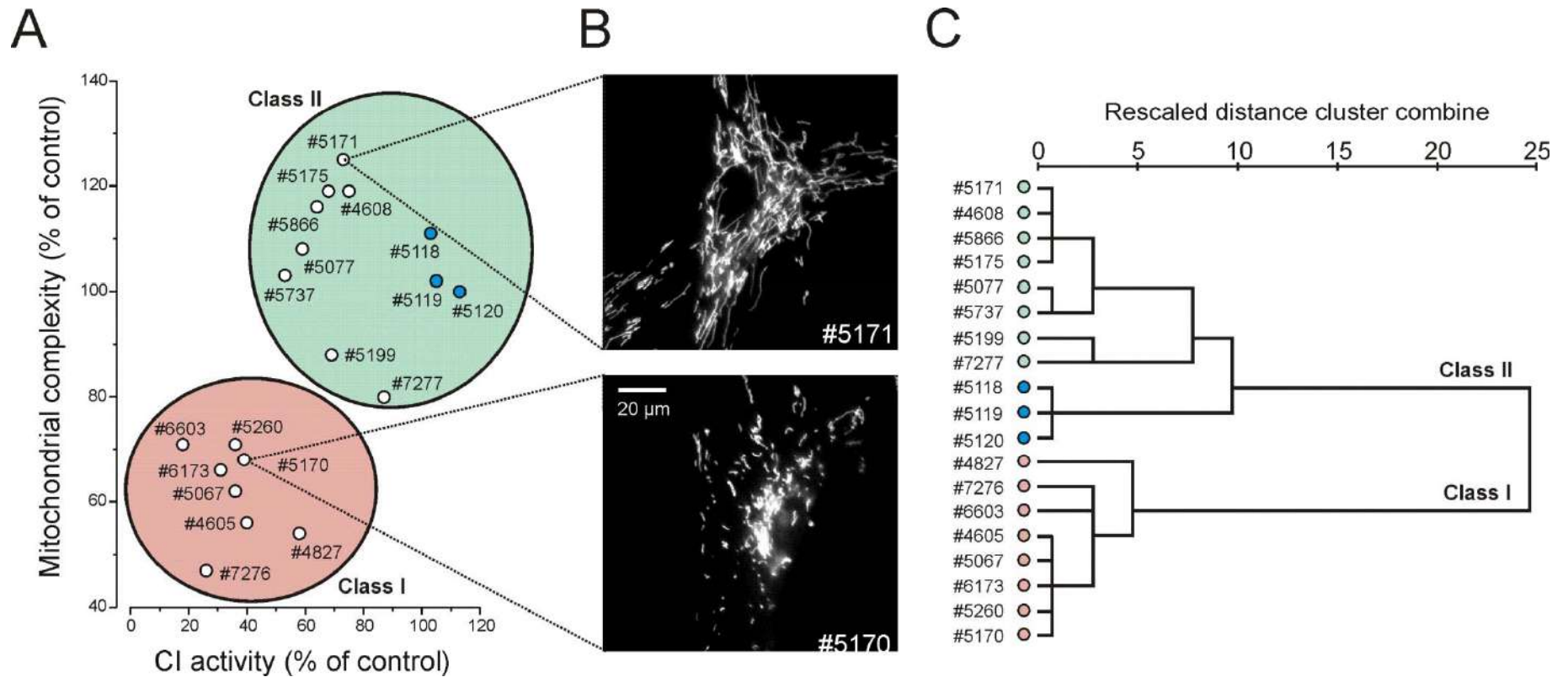
Control



Patient: Filamentous

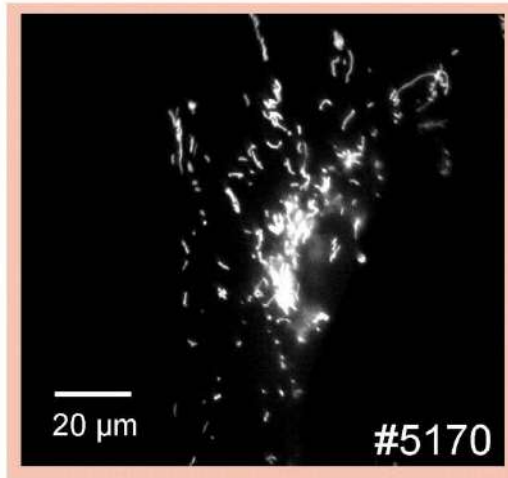


Mitochondrial morphology correlates with residual complex I activity

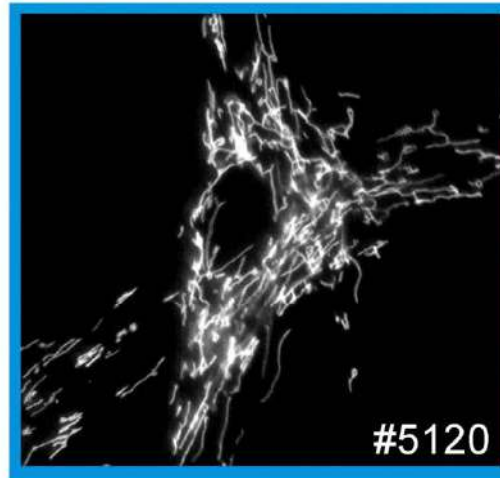


A 'good' mitochondrial structure relates to better mitochondrial function and less ROS

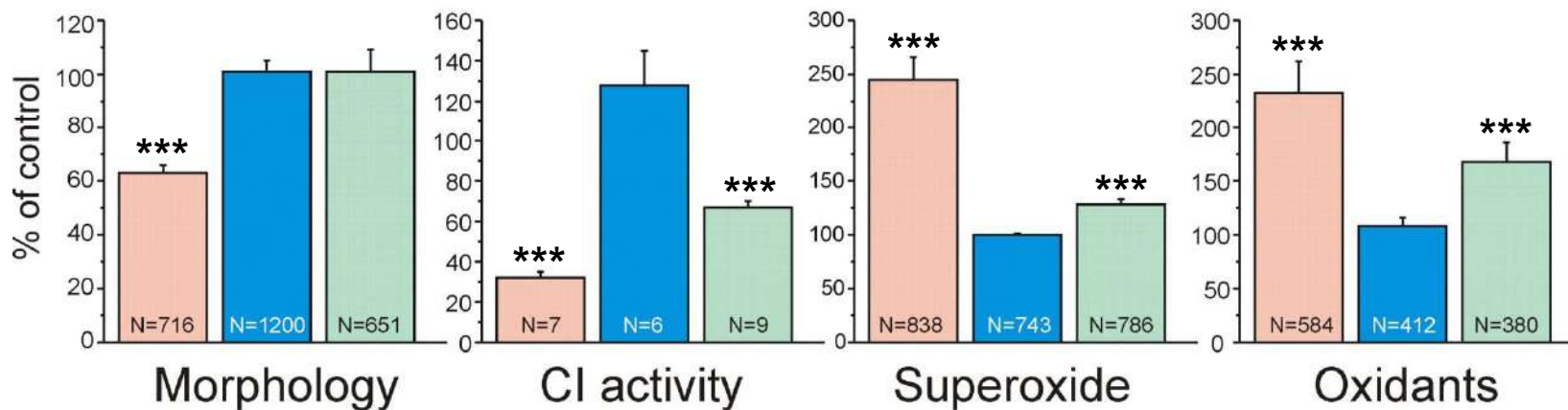
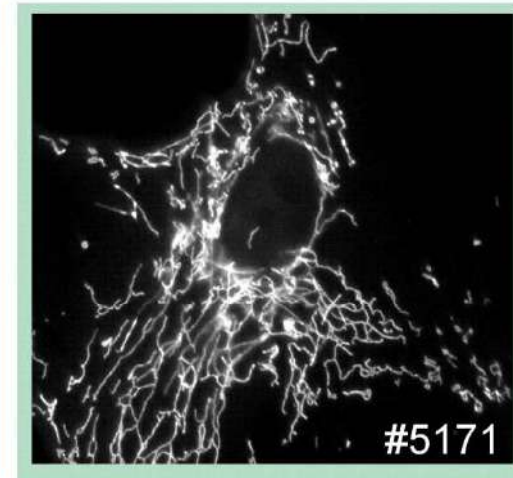
Patient: fragmented



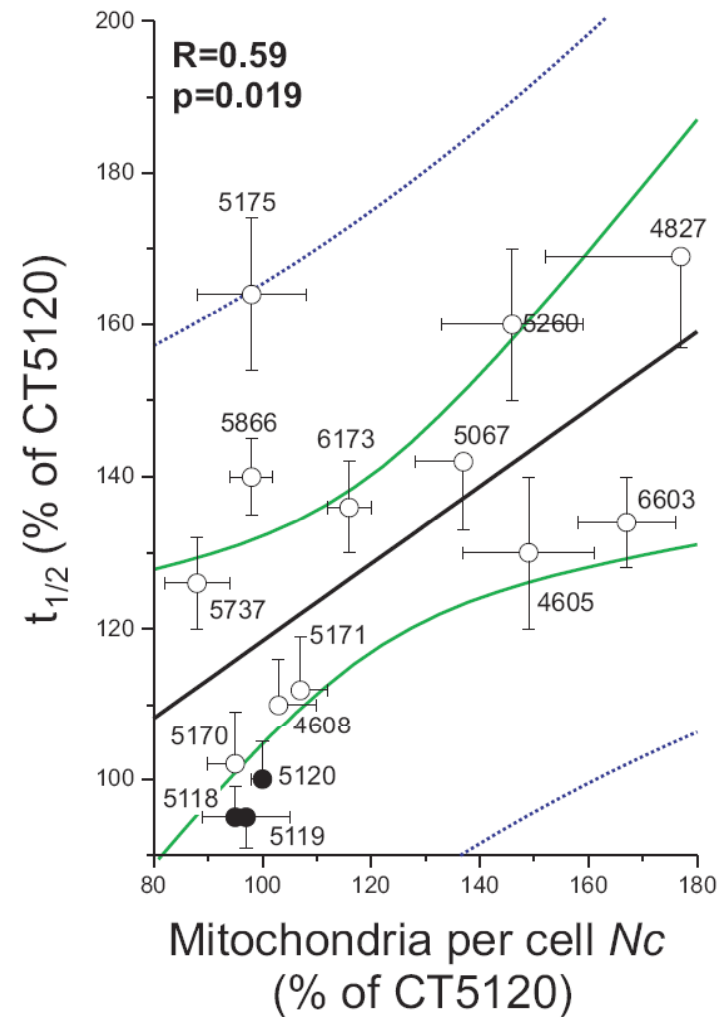
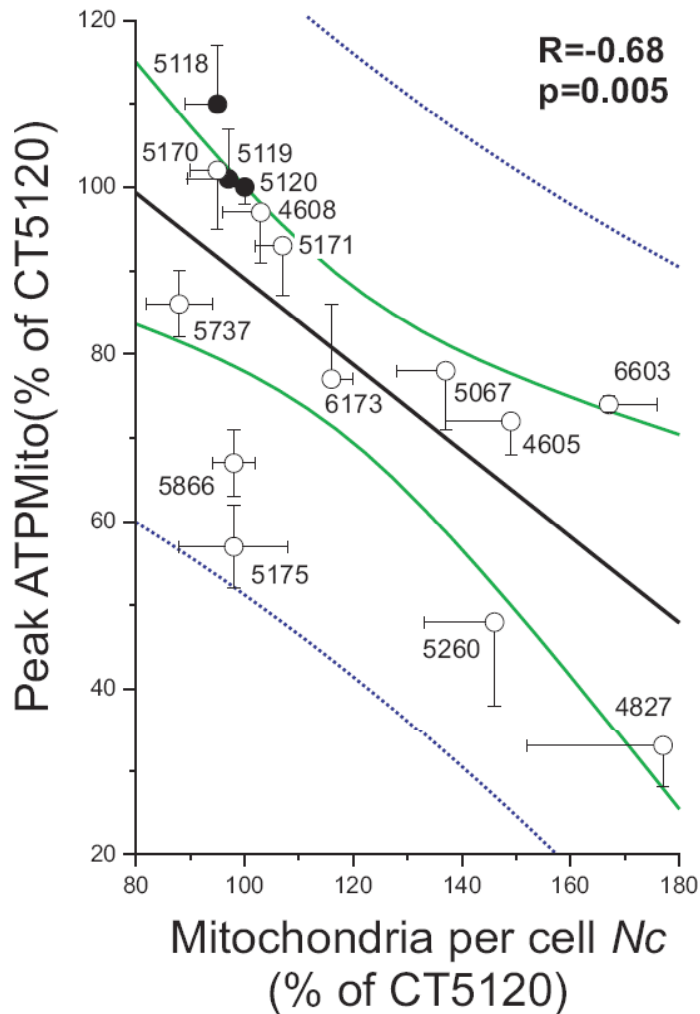
Control



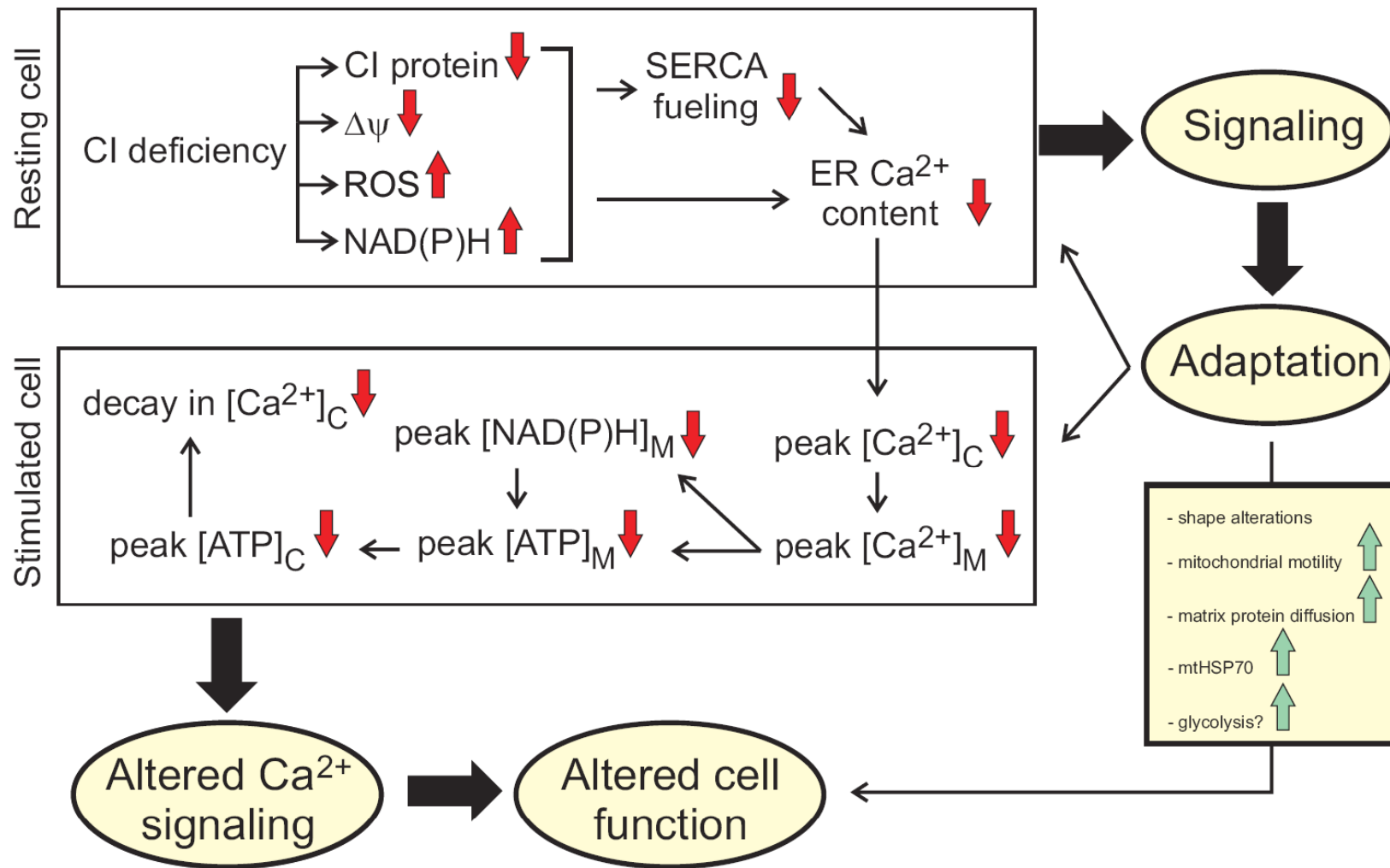
Patient: Filamentous



The number of mitochondria per cell relates to mitochondrial Ca^{2+} /ATP handling

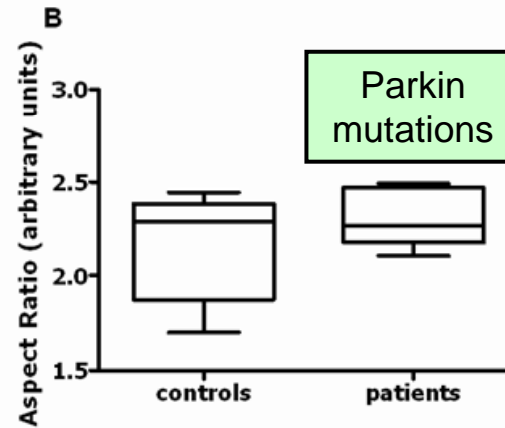
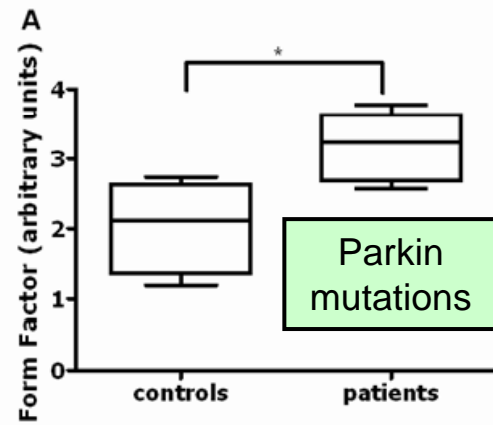


Cell biological consequences of human complex I deficiency

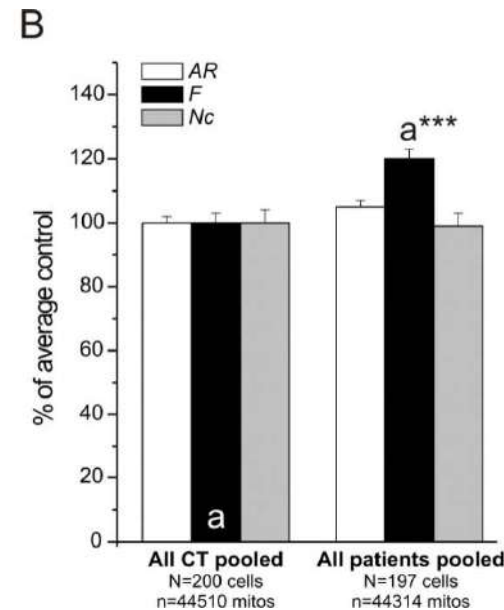
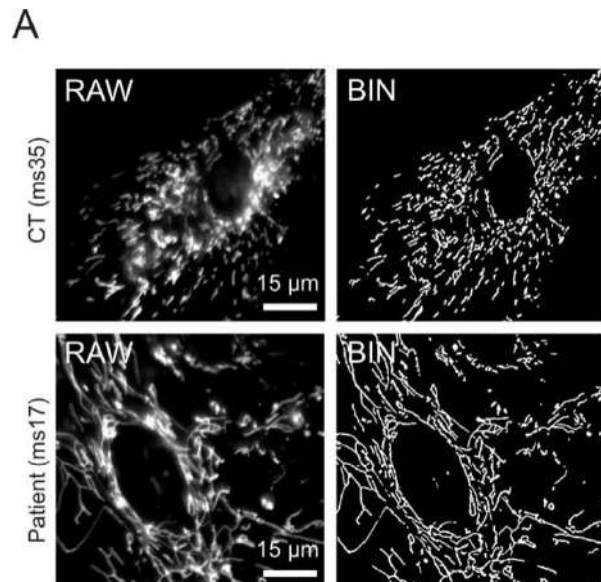




Mitochondria become more branched in Parkinson's disease and HIBM

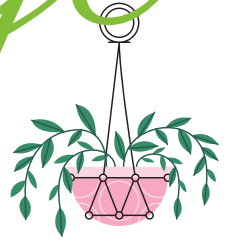


Fibroblast from patients with Parkinson's disease



Myoblasts from patients with Hereditary Inclusion Body Myopathy

Bon courage



LIENS UTILES 🙌

Visiter :

1. <https://biologie-maroc.com>

- Télécharger des cours, TD, TP et examens résolus (PDF Gratuit)

2. <https://biologie-maroc.com/shop/>

- Acheter des cahiers personnalisés + Lexiques et notions.
- Trouver des cadeaux et accessoires pour biologistes et géologues.
- Trouver des bourses et des écoles privées

3. <https://biologie-maroc.com/emploi/>

- Télécharger des exemples des CV, lettres de motivation, demandes de ...
- Trouver des offres d'emploi et de stage

