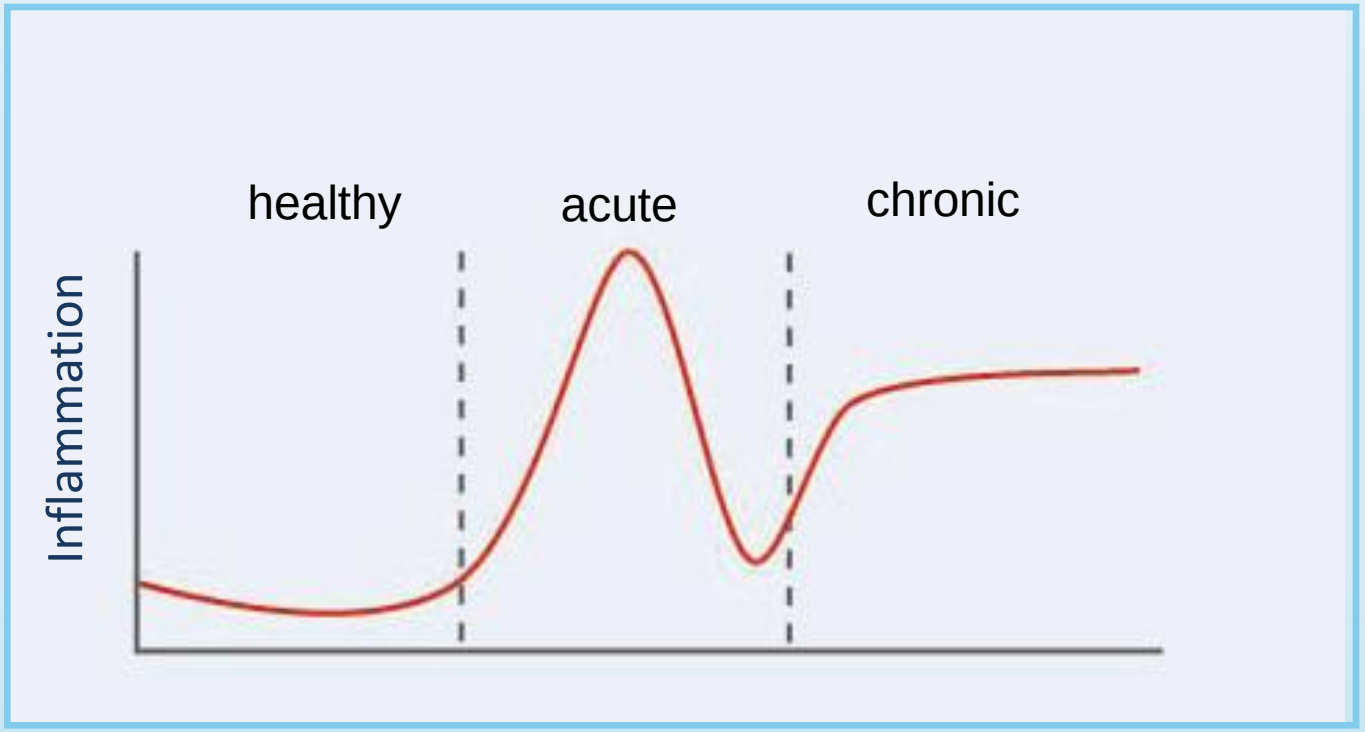
First Congress

International Society of Diamagnetic Therapy

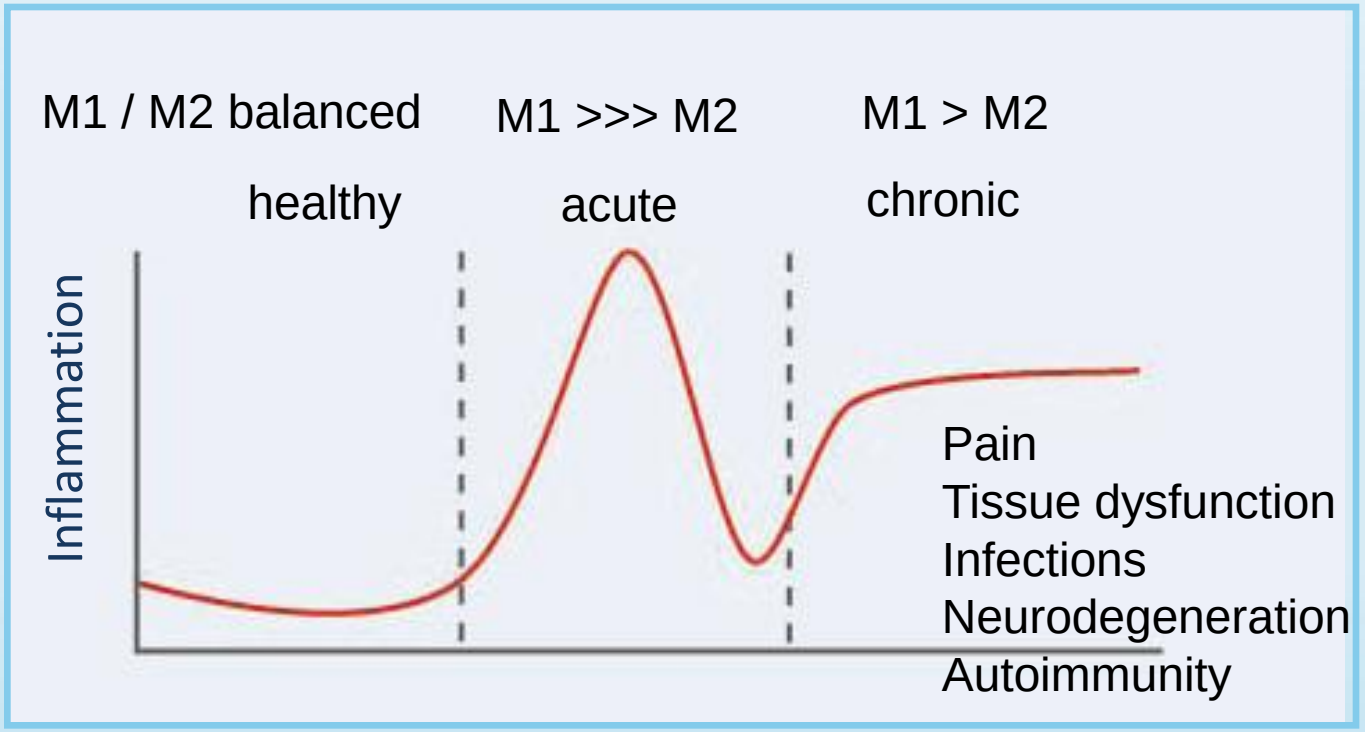
Cell Membrane Stimulation and Phagocytic Capacity by Diamagnetic Effect

Marion Schneider
Clinic of Neurology Ulm
University Hospital

13th – 14th September 2024
Magna Graecia University - Catanzaro



Fei Chen and Vince Catranova Cancer Research 2007; 67:(23), Dec, 2007



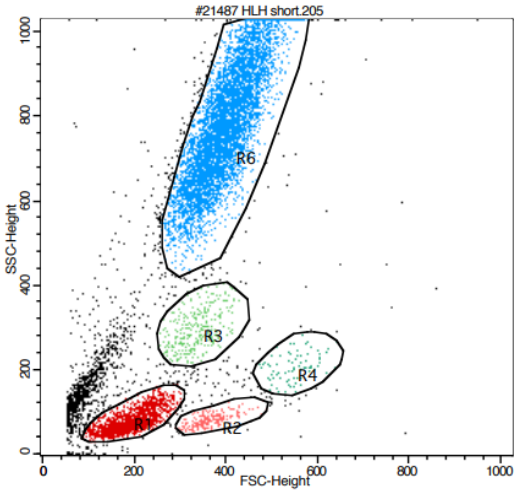
Fei Chen and Vince Catranova Cancer Research 2007; 67:(23), Dec, 2007

In vivo treatment of healthy donors flow cytometric analysis

Flow cytometric analysis of blood leukocytes

Gate: No Gate
Gated Events: 10000
Total Events: 10000

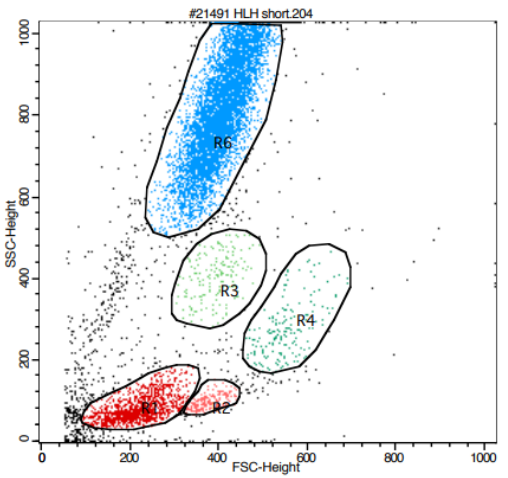
Gate	Events	% Gated	% Total
Lymphozyten A	1744	17.44	17.44
Lymphozyten B	206	2.06	2.06
Monozyten A	293	2.93	2.93
Monozyten B	81	0.81	0.81
Granulozyten B	6314	63.14	63.14



Leukocytes donor MJ

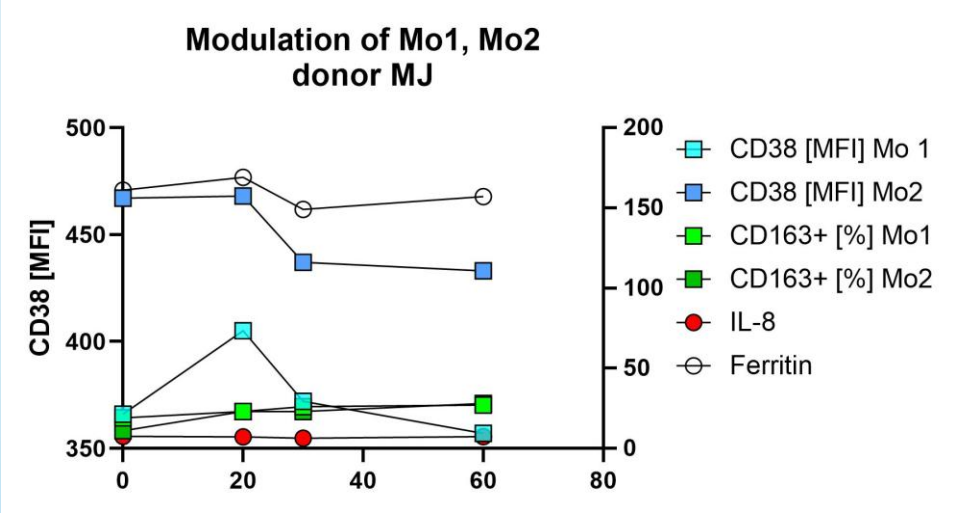
Gate: No Gate
Gated Events: 10000
Total Events: 10000

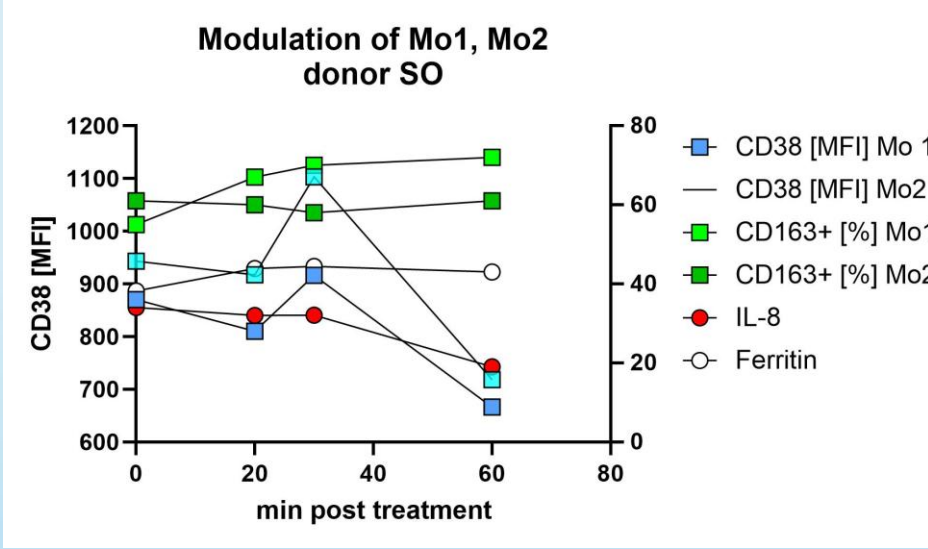
Gate	Events	% Gated	% Total
Lymphozyten A	1281	12.81	12.81
Lymphozyten B	209	2.09	2.09
Monozyten A	172	1.72	1.72
Monozyten B	179	1.79	1.79
Granulozyten B	6496	64.96	64.96



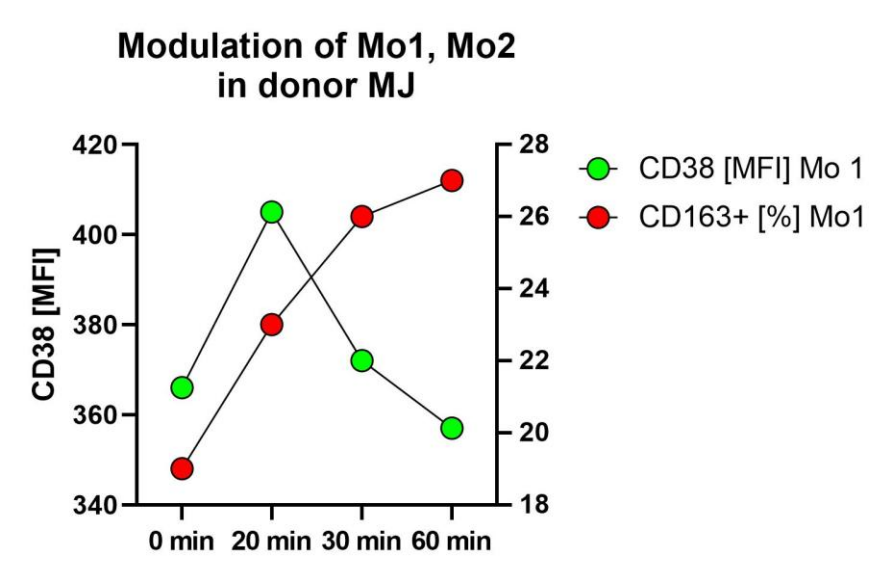
Leukocytes donor SO

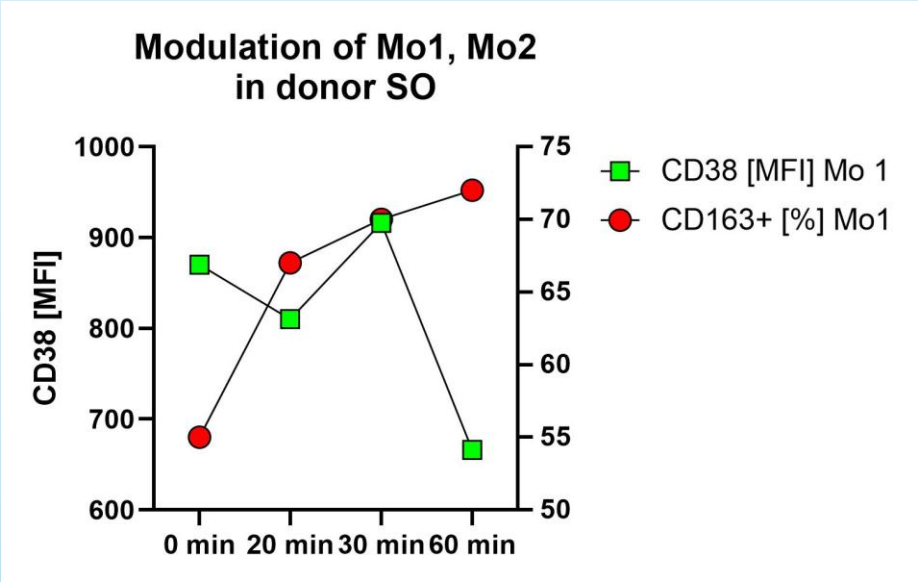
Monocyte subtypes after Vagus nerve stimulation



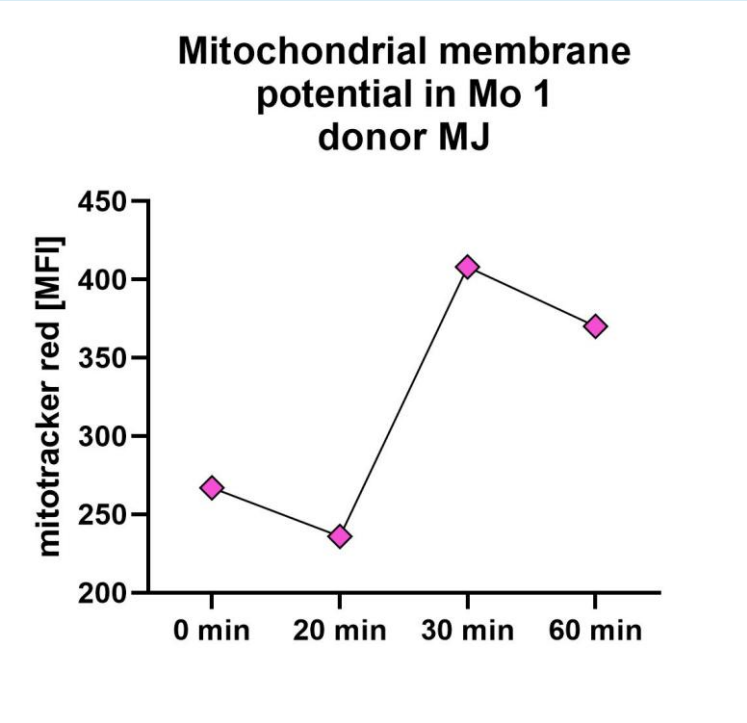


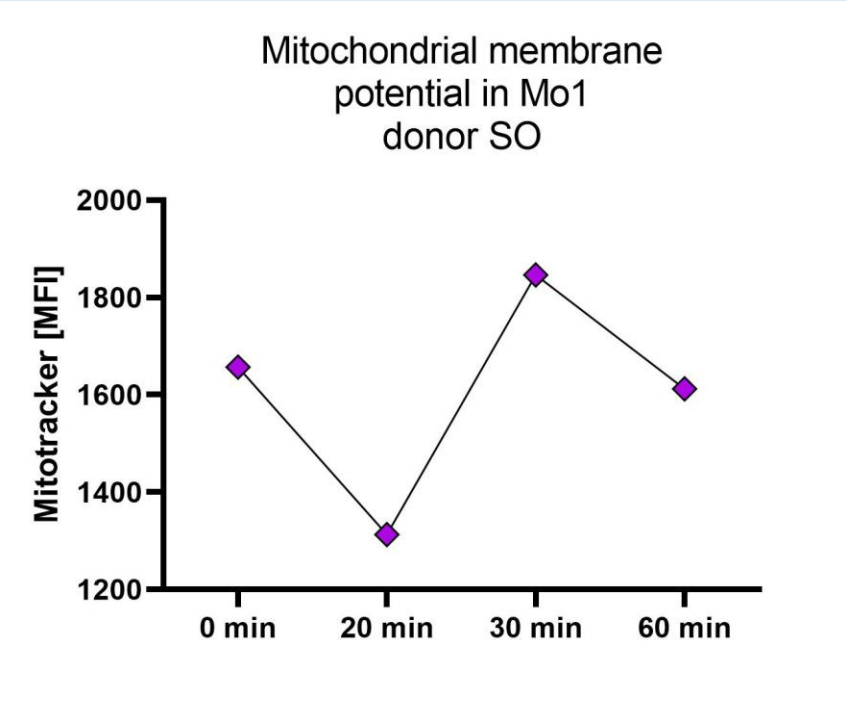
M1 – M2 Balance following CTU mega 20



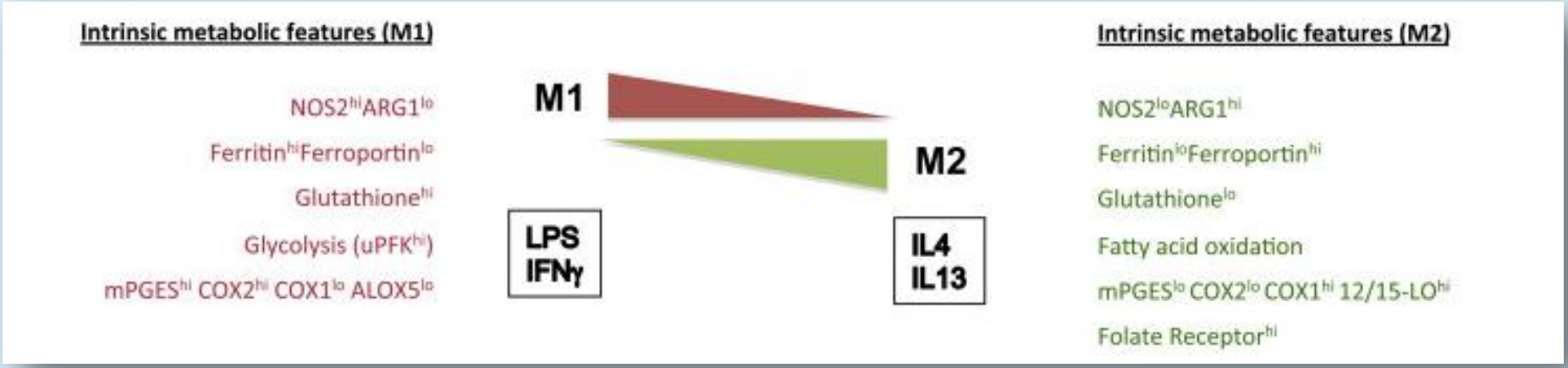


Kinetics of mitochondrial membrane potential in monocytes after diamagnetic therapy





Metabolic properties in M1 and M2 macrophages



CD38^{++}

Ferritin

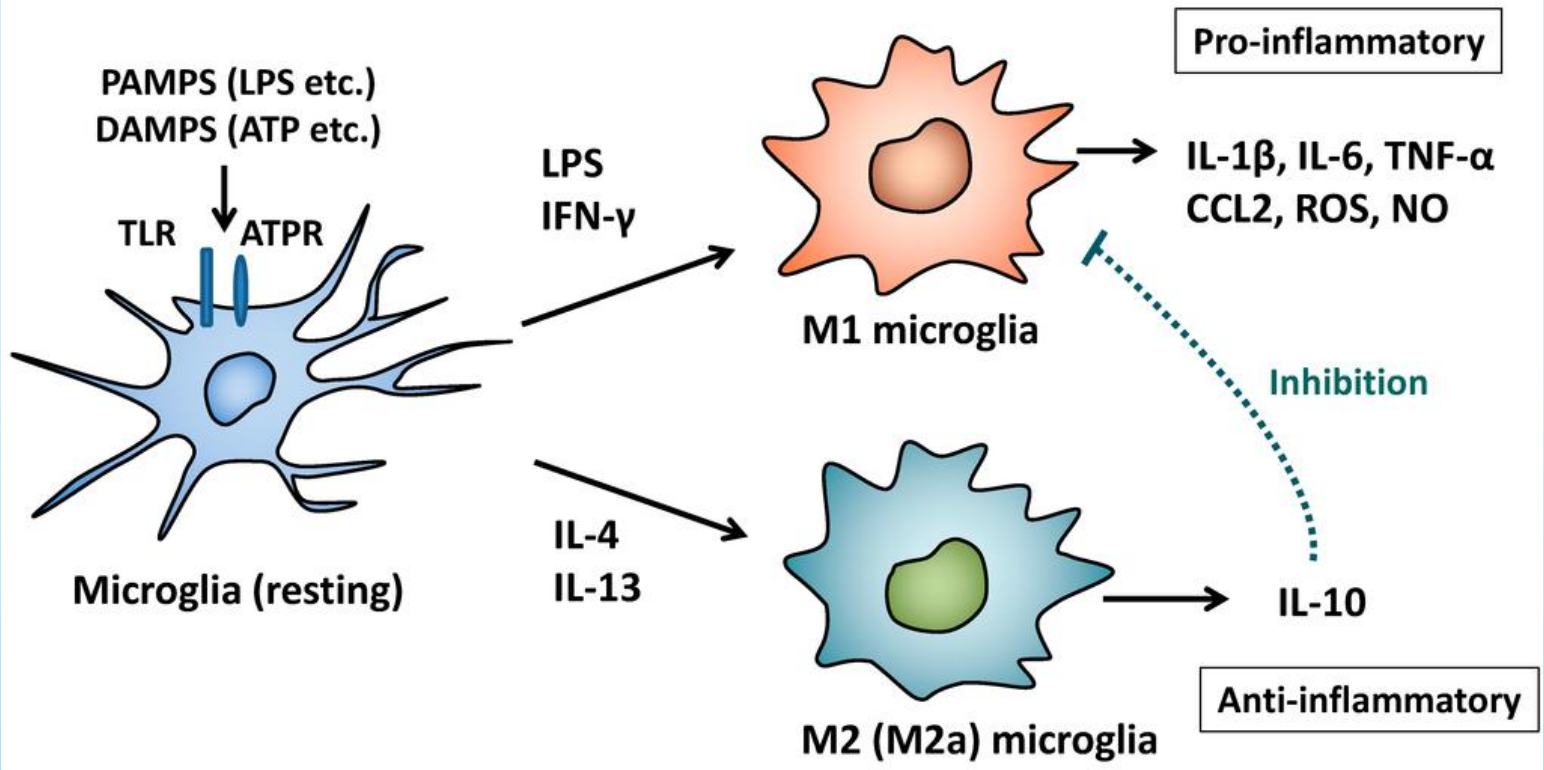
IL-1β

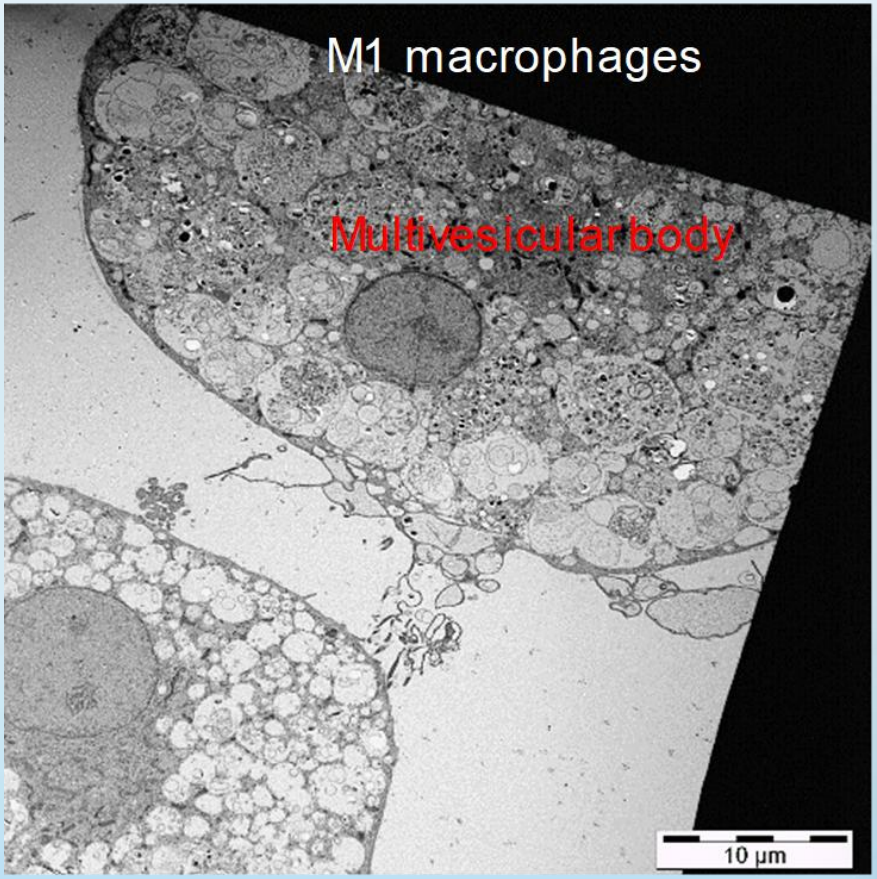
CD163^{++}

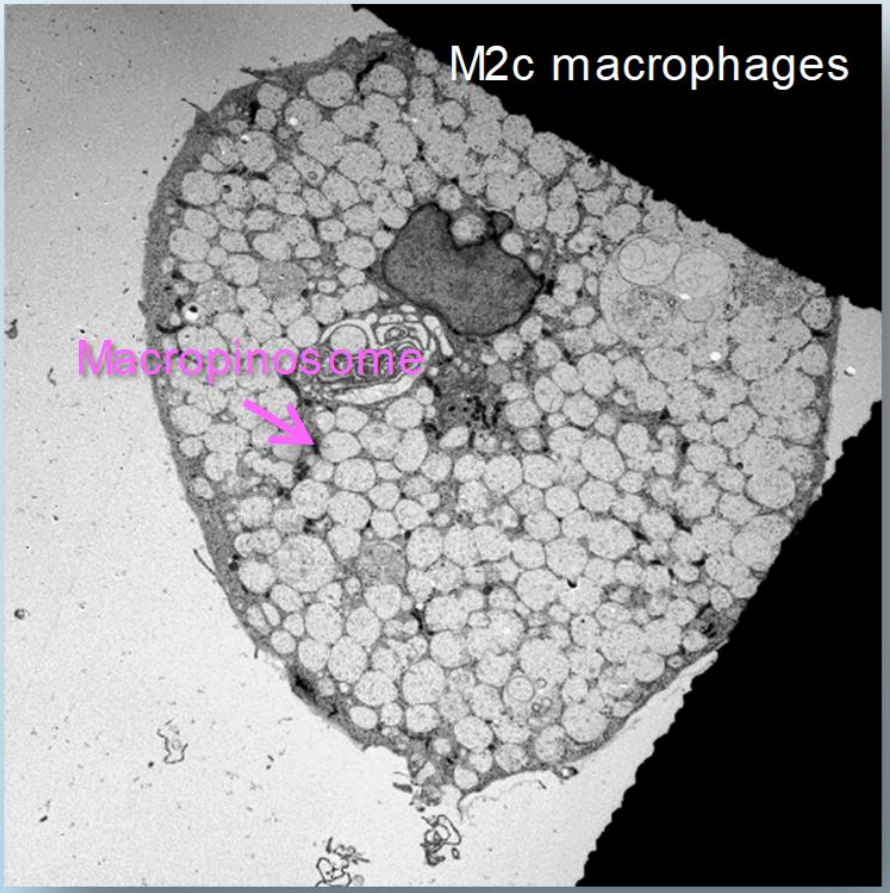
M-CSF

Orchestration of Metabolism by Macrophages
Subhra K. Biswas1,* and Alberto Mantovani2,*

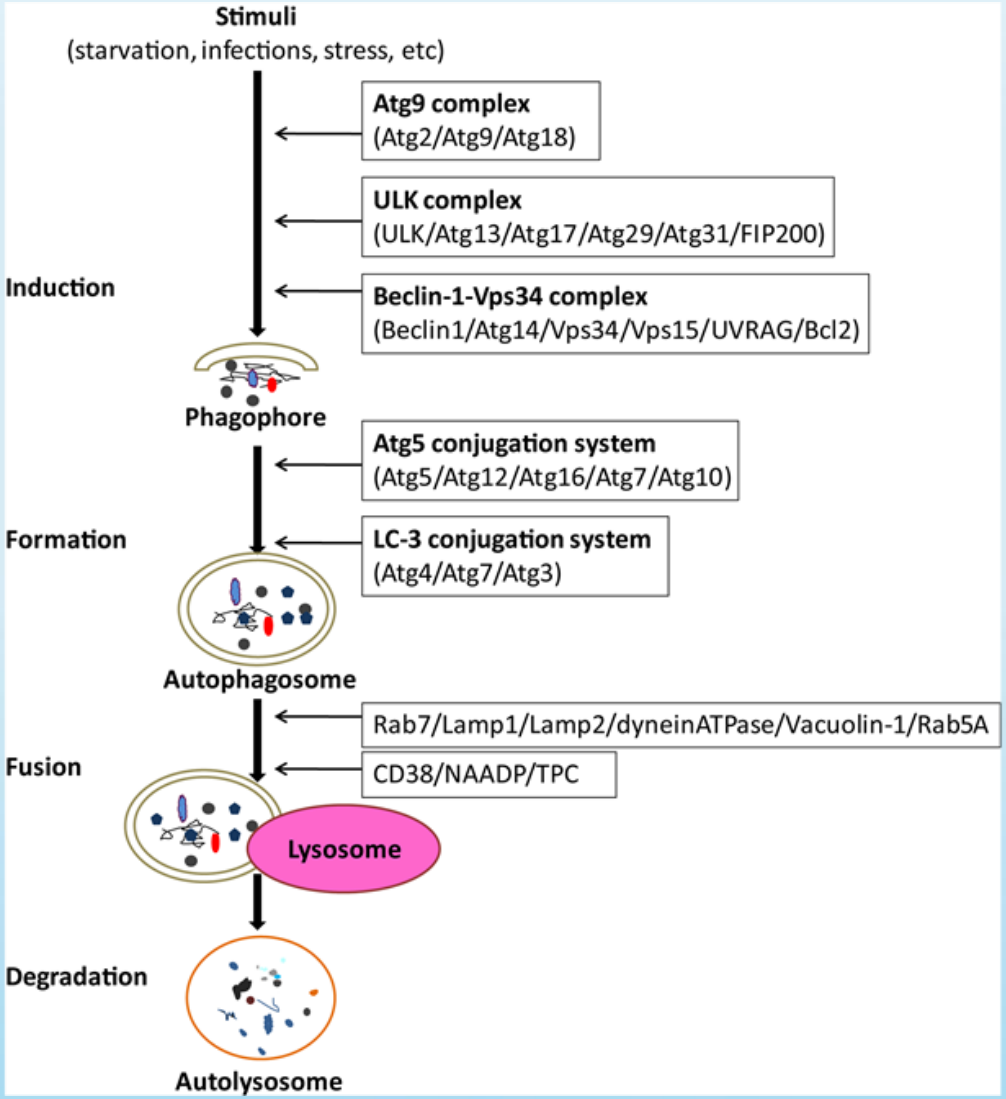
M1 / M2 phenotypes in the brain




M1 macrophages
Multivesicular body
10 µm


M2c macrophages
Macropinosome

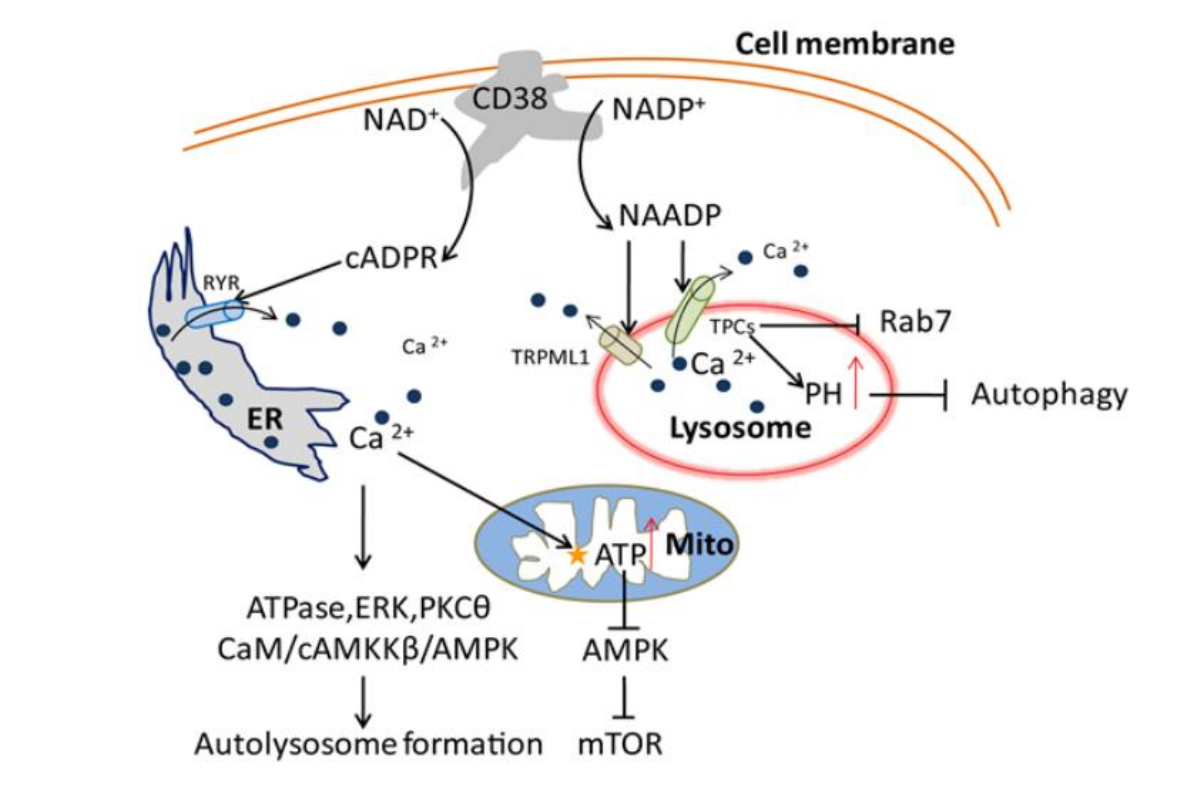
CD38



Wang, X.W., Song J.X., Wu, Z.J., Fan, B.Q. and Mode X.M. (2017) Dual Roles of CD38 in Autophagy. Yangtze Medicine, 1, 8-19. https://doi.org/10.4236/ym.2017.11002

CD38

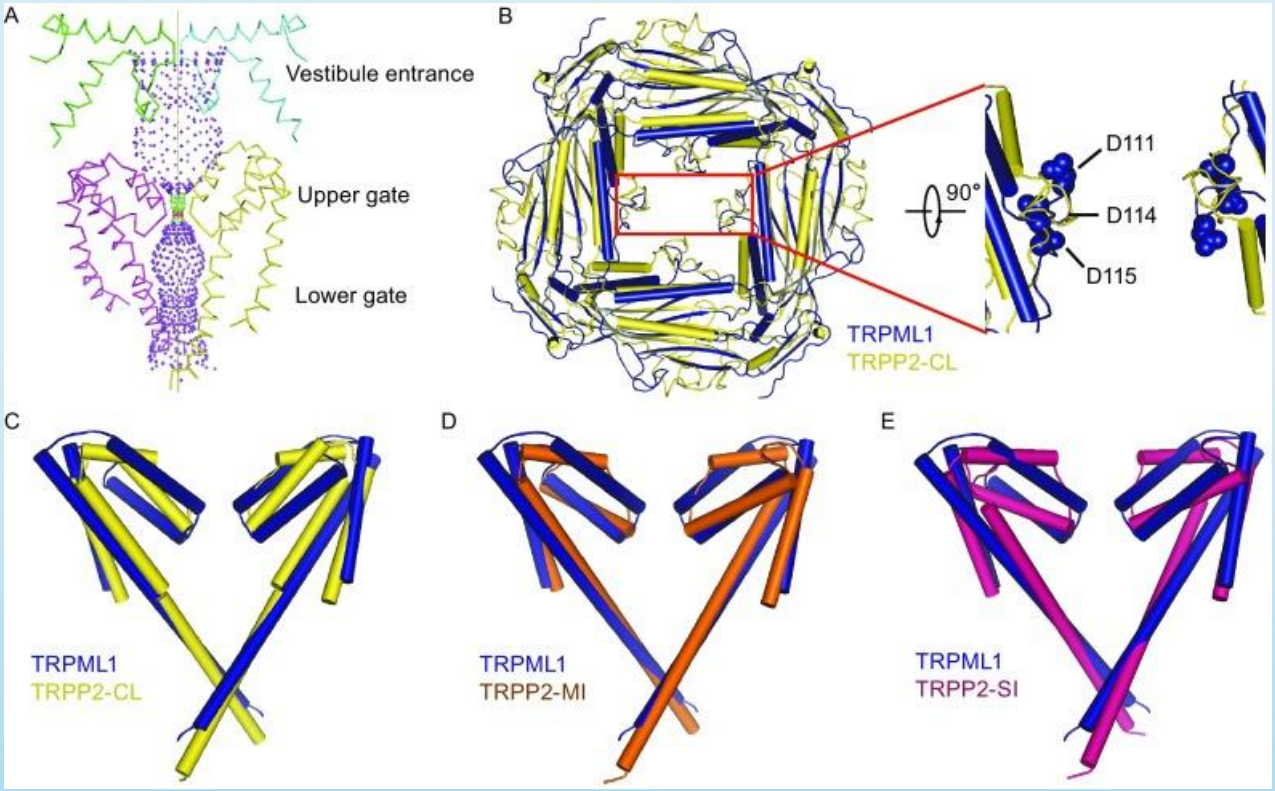
CD38 is responsible for the synthesis of cADPR (cyclic ADP-ribose) and nicotinic acid adenine dinucleotide phosphate (NAADP) which serve as important intracellular Ca^{2+} messengers, for intracellular Ca^{2+} flux from either ER or endolysosome



Wang, X.W., Song J.X., Wu, Z.J., Fan, B.Q. and Mode X.M. (2017) Dual Roles of CD38 in Autophagy. Yangtze Medicine, 1, 8-19. https://doi.org/10.4236/ym.2017.11002

CD38

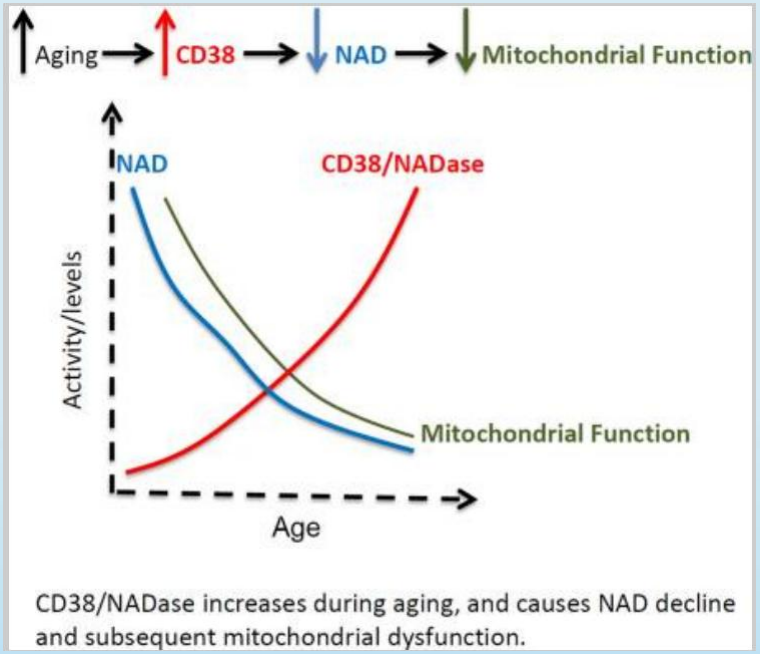
NAADP drives Ca^{2+} flux from the endolysosomal pools by targeting the two-pore channels (TPCs) or transient receptor potential mucolipin-1 (TRPML1)



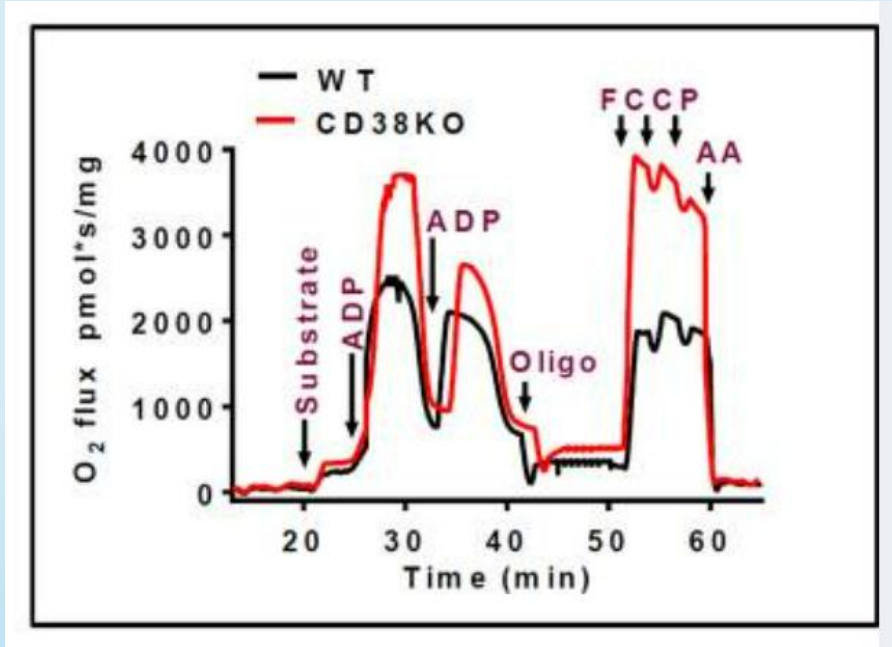
Zhang S, Li N, Zeng W, Gao N, Yang M. Cryo-EM structures of the mammalian endo-lysosomal TRPML1 channel elucidate the combined regulation mechanism. Protein Cell. 2017 Nov;8(11):834-847. doi: 10.1007/s13238-017-0476-5. Epub 2017 Sep 21. PMID: 28936784; PMCID: PMC5676595.

CD38 and NAD

CD38 is one of the main NAD-degrading enzymes in mammalian tissues and dictates aging[8]



CD38/NADase increases during aging, and causes NAD decline and subsequent mitochondrial dysfunction.



Camacho-Pereira J, Tarragó MG, Chini CCS, Nin V, Escande C, Warner GM, Puranik AS, Schoon RA, Reid JM, Galina A, Chini EN. CD38 Dictates Age-Related NAD Decline and Mitochondrial Dysfunction through an SIRT3-Dependent Mechanism. Cell Metab. 2016 Jun 14;23(6):1127-1139. doi: 10.1016/j.cmet.2016.05.006. PMID: 27304511; PMCID: PMC4911708.

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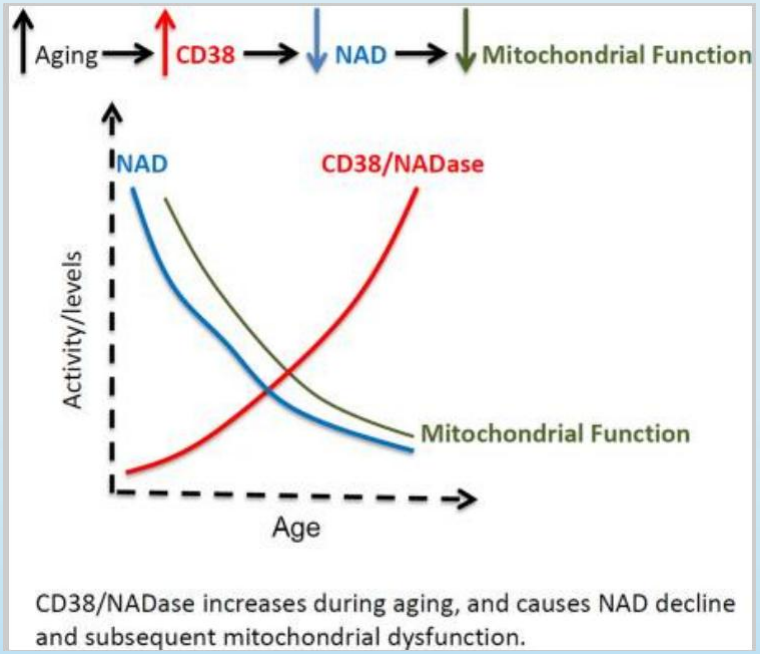

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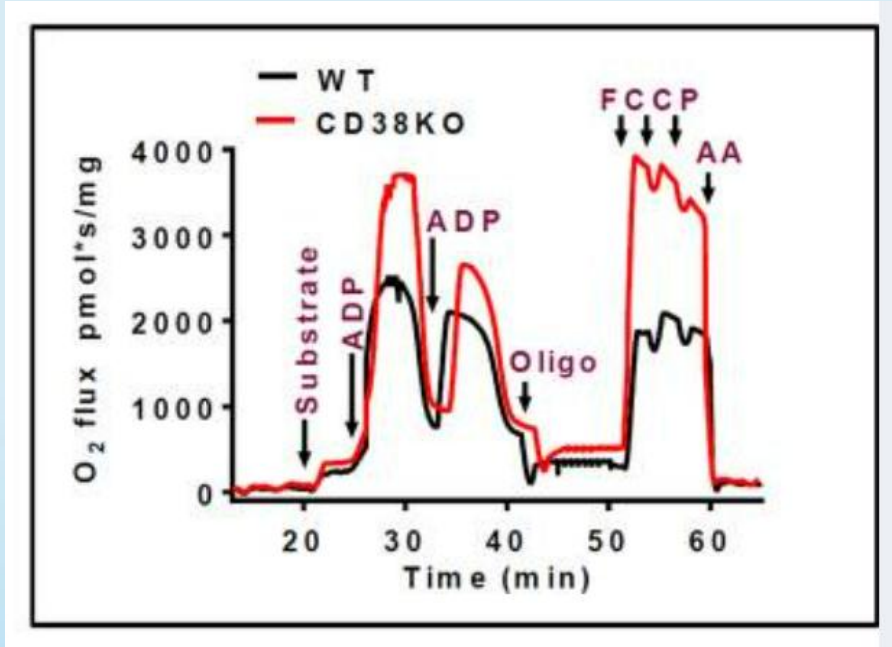

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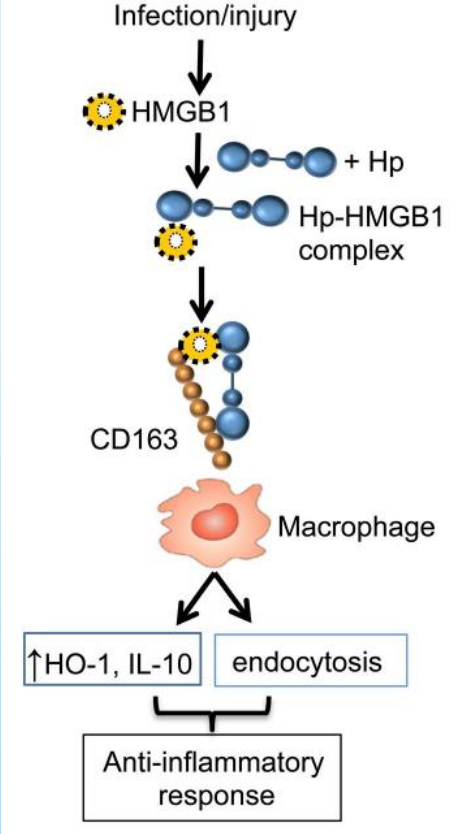
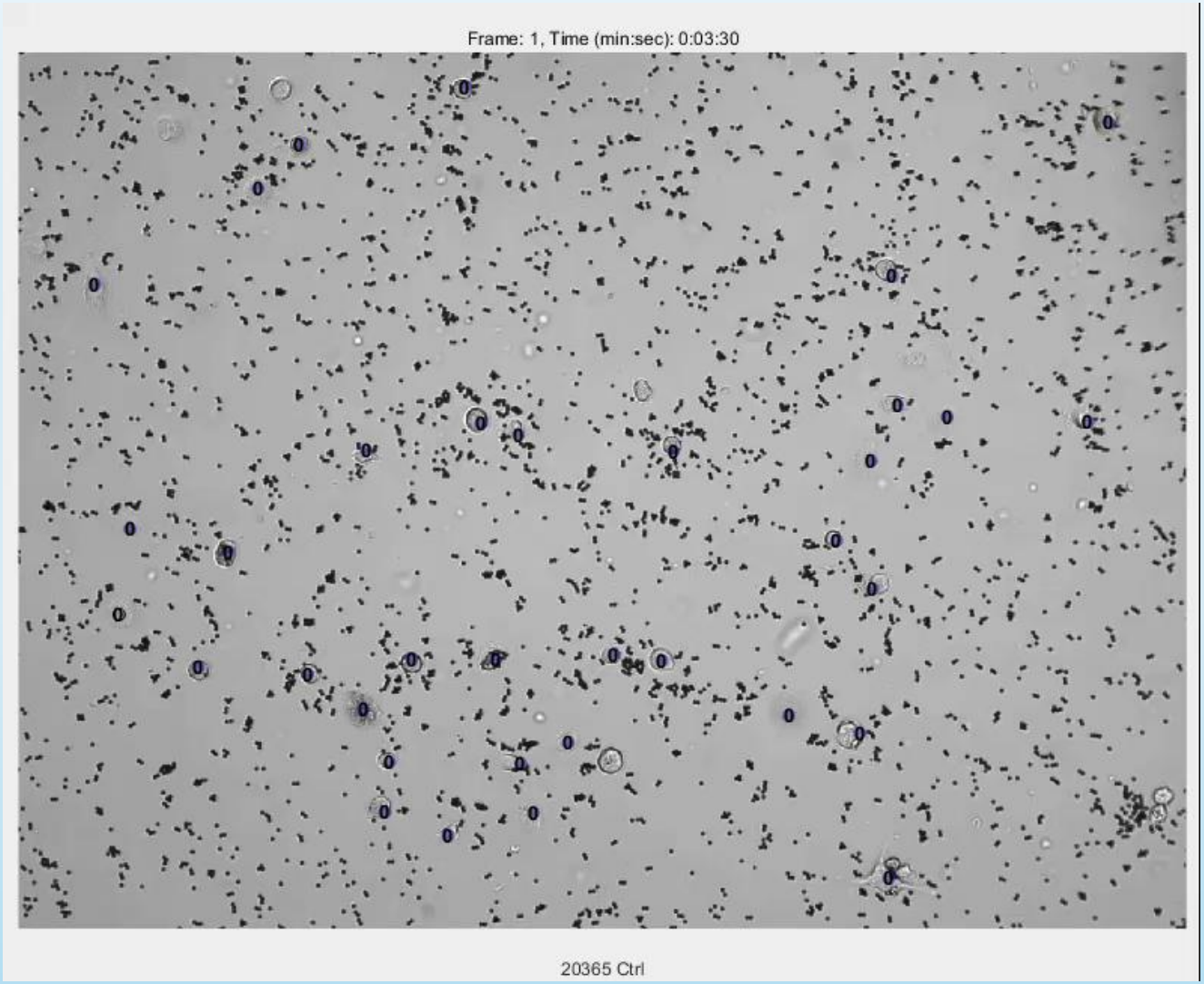
CD163

CD163 is an important scavenger receptor on tissue repair macrophages. The receptor binds hemoglobine/haptoglobine complexes as well as HMGB-1 and intitiates an anti-inflammatory cascade.



JCI Insight. 2016;1(7):e85375. https://doi.org/10.1172/jci.insight.85375.

Monitoring phagocytosis by Dynal Bead uptake



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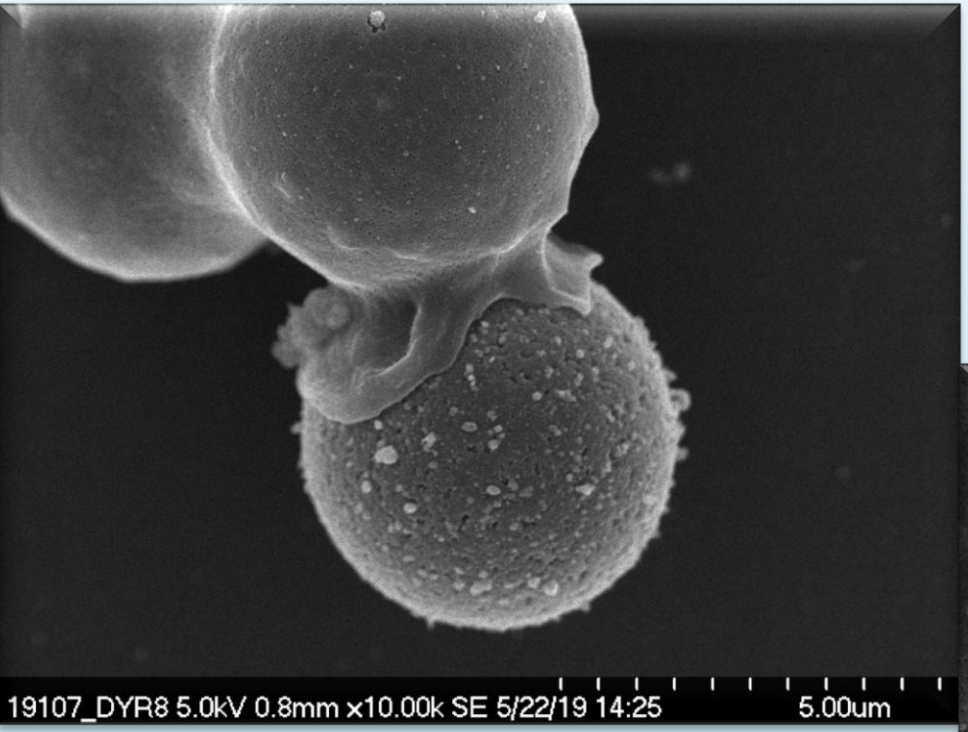
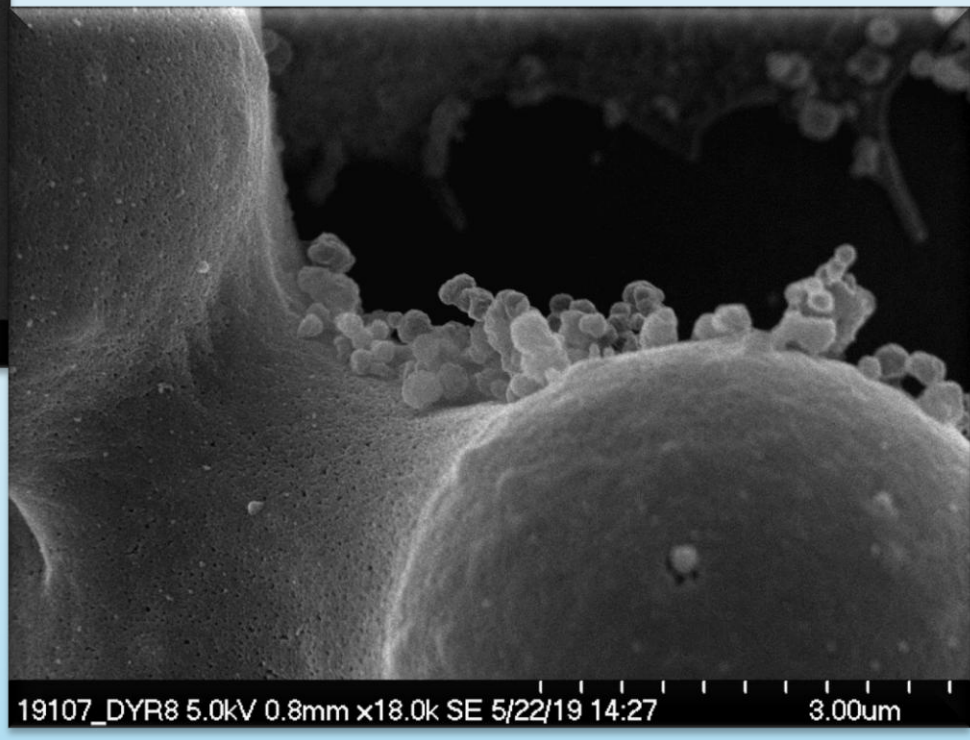
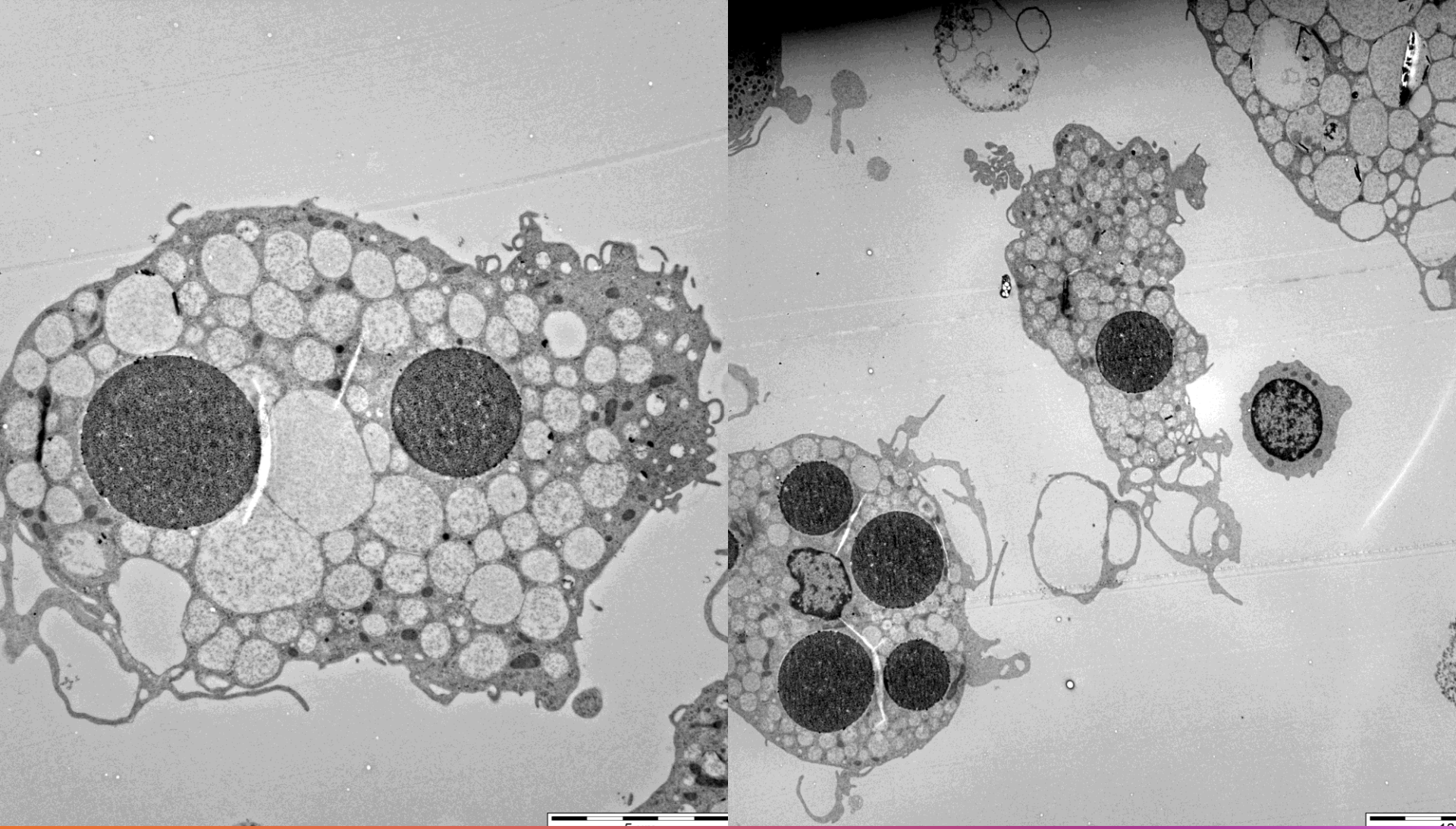
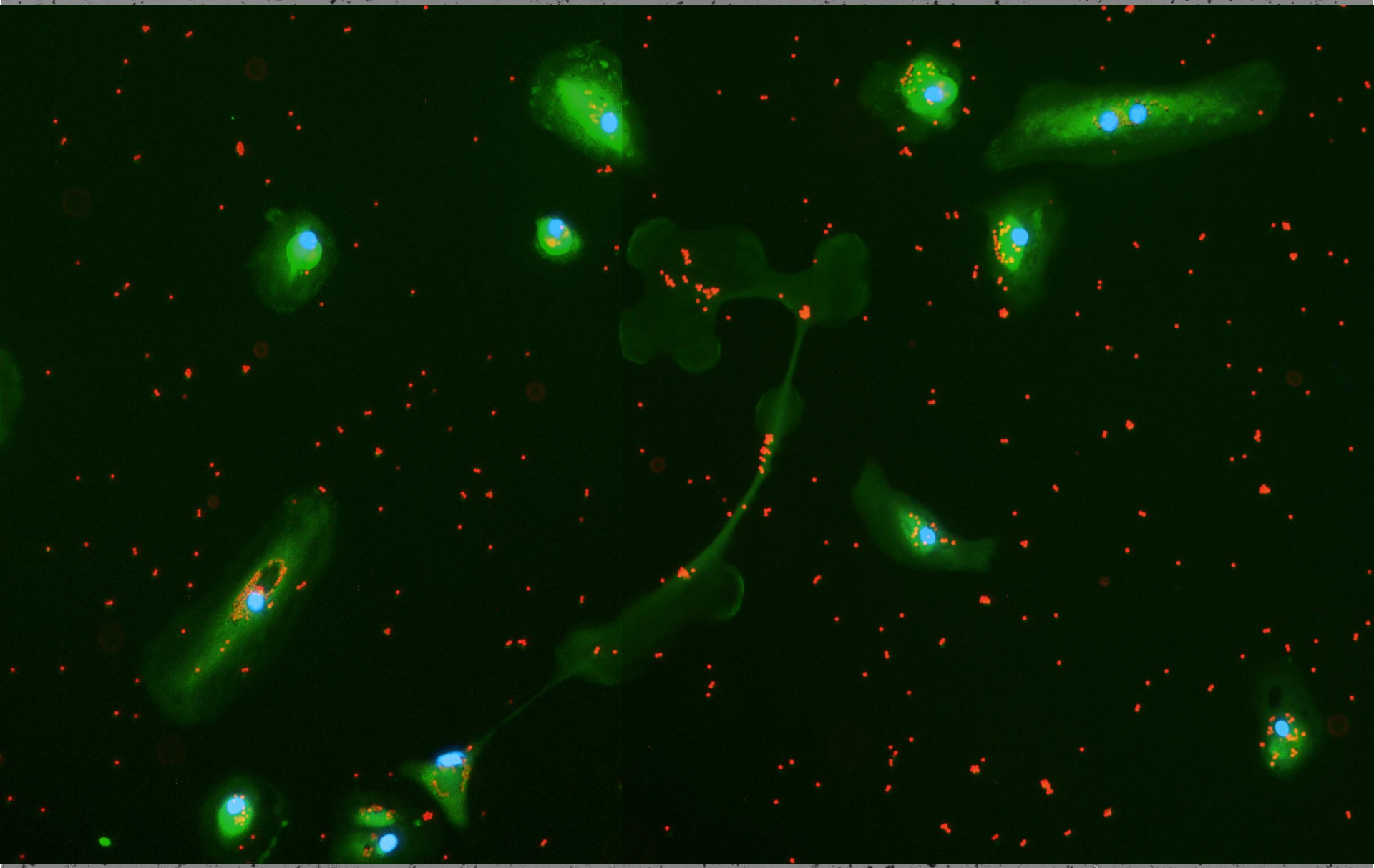
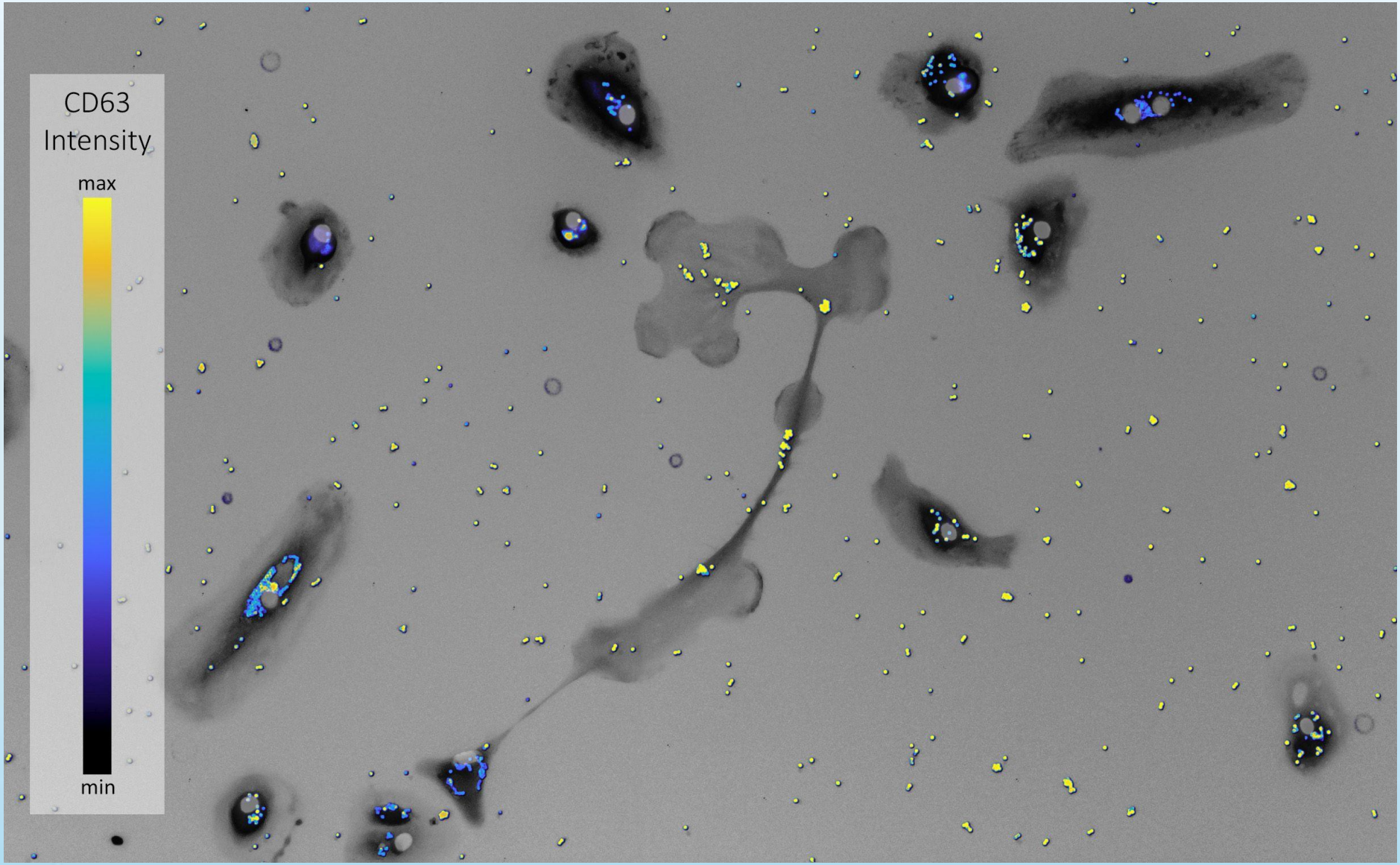


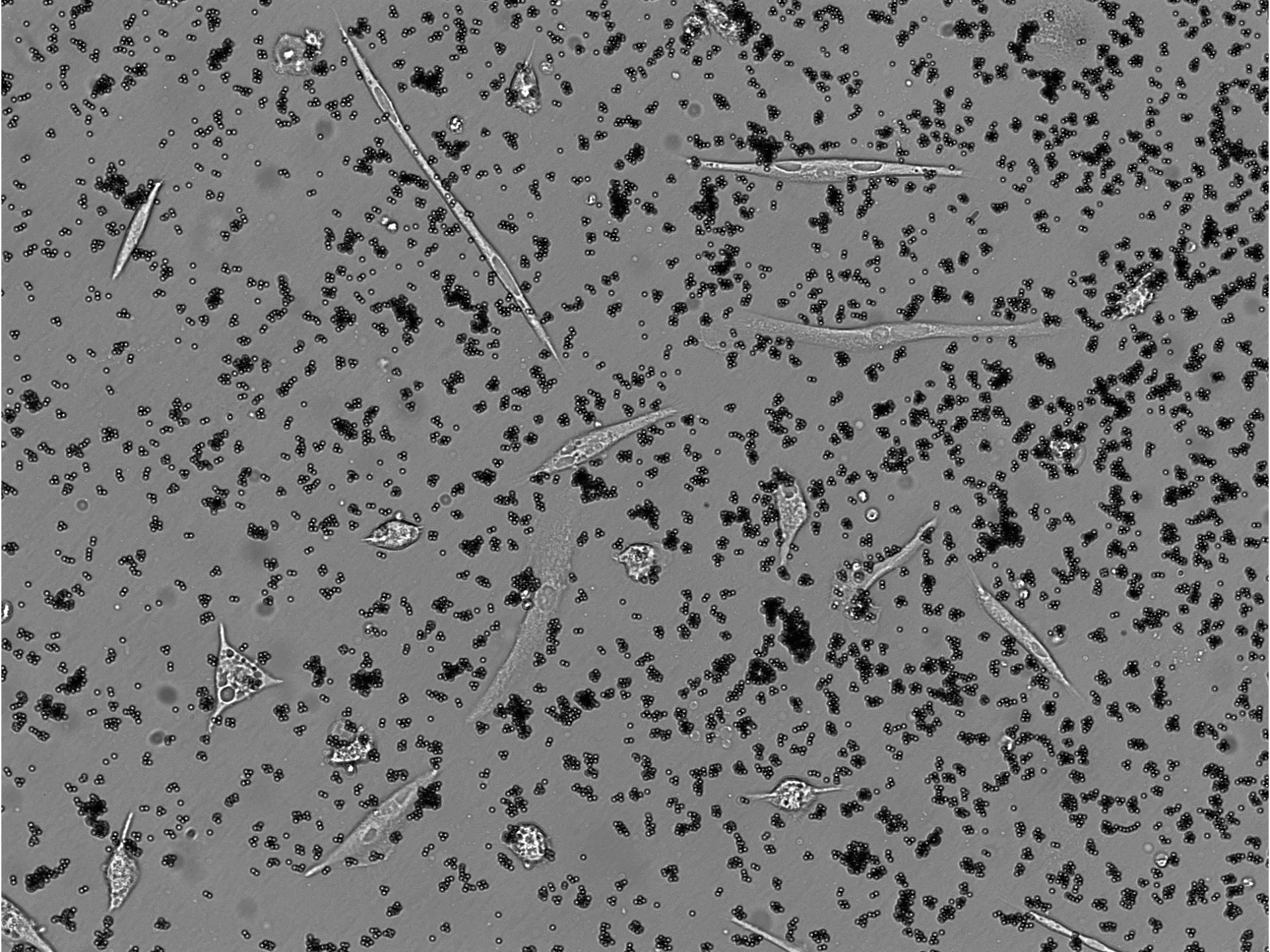


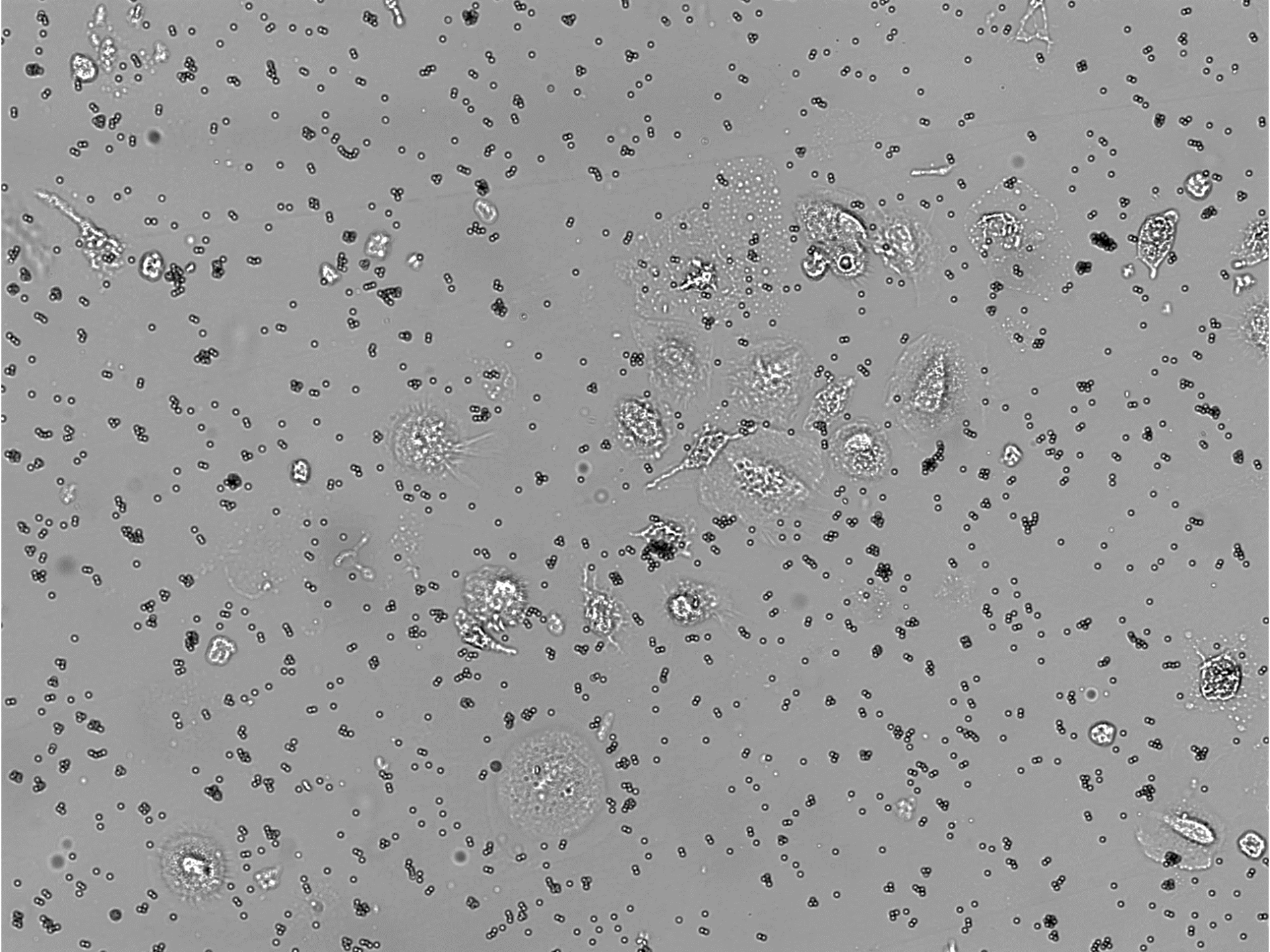




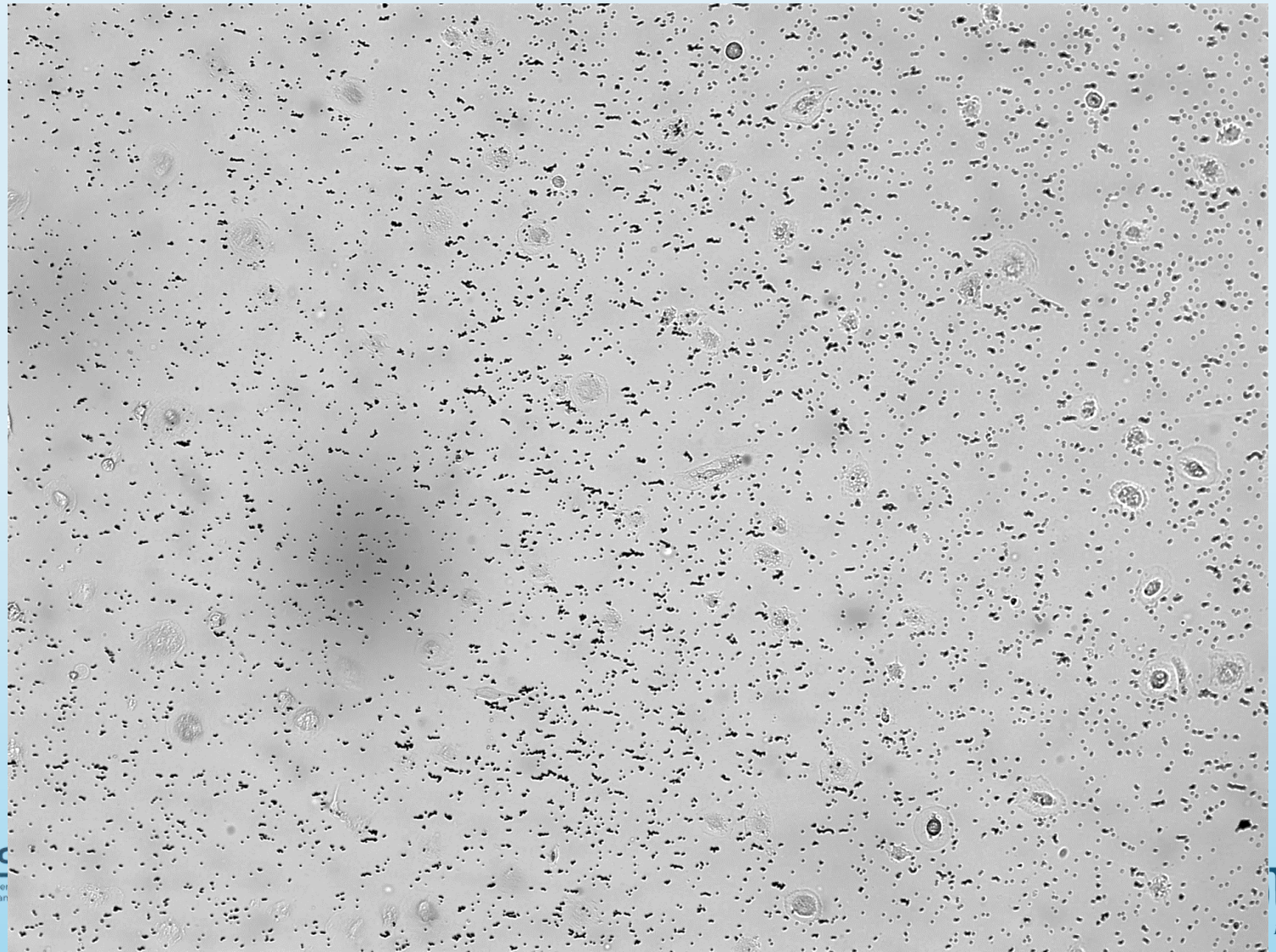
Emperilopoesis/digestion of internalized Dynal Beads







Dynal beads orientation upon CTUmega20 treatment



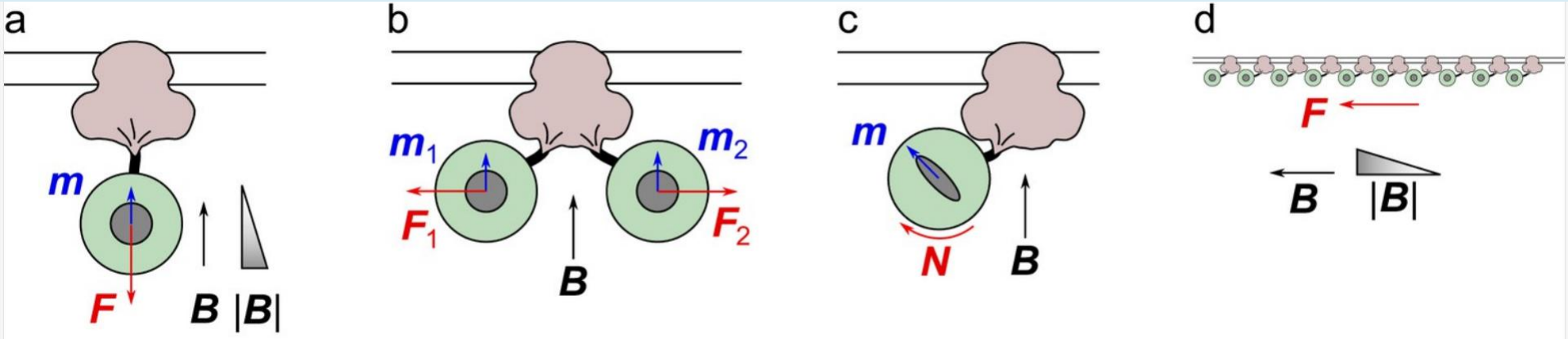
Unraveling magnetogenetics

Magnetogenetics has just emerged as a way to noninvasively activate neurons.

Targeting the iron-binding protein ferritin to TRP channels in the neuronal membrane. A magnetic field is then thought either to exert a magnetic force on ferritin complexes or to heat the iron-containing complexes, both of which would open up the associated TRP channels and result in neuronal activation

Vogt, N. Unraveling magnetogenetics. *Nat Methods* **13**, 901 (2016). https://doi.org/10.1038/nmeth.4060

Hypothetical membrane complex of ferritin with TRPV4



A TRPV4 channel (pink) inserted in the membrane with a ferritin complex (green) attached on the cytoplasmic side, approximately to scale.
The magnetic field ***B*** induces a moment ***m*** in the ferritin core, leading to a force ***F*** or a torque ***N*** on the ferritin particle, and resulting forces tugging on the channel. See text for details.
https://doi.org/10.7554/eLife.17210.003

Iron distribution in the rat brain

Arch Histol Cytol, 71 (4): 205-222 (2008)

Cellular and subcellular localizations of nonheme ferric and ferrous iron in the rat brain: a light and electron microscopic study by the perfusion-Perls and -Turnbull methods*

Reiko Meguro, Yoshiya Asano, Saori Odagiri, Chengtai Li, and Kazuhiko Shoumura

Department of Neuroanatomy, Cell Biology and Histology, Hirosaki University Graduate School of Medicine, Hirosaki, Japan

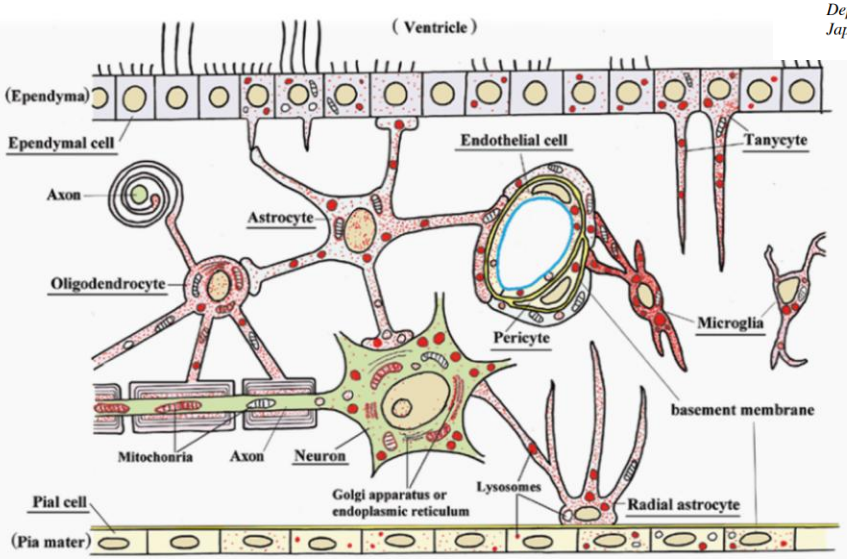


Fig. 9. Illustration of the subcellular distribution of nonheme iron in the rat brain. Red indicates a nonheme iron, mainly Fe(III), positive reaction. The red dot density is roughly proportional to the density of the iron positive reaction subcellularly. Blue indicates a Fe(II)-positive reaction; yellow indicates the basement membrane.

…”Even with a 100-fold larger field (5 T), these forces are still 4 log units too small to open a channel….”.

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SHORT REPORT

Physical limits to magnetogenetics

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Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, United States

Abstract This is an analysis of how magnetic fields affect biological molecules and cells. It was prompted by a series of prominent reports regarding magnetism in biological systems. The first claims to have identified a protein complex that acts like a compass needle to guide magnetic orientation in animals (*Qin et al., 2016*). Two other articles report magnetic control of membrane conductance by attaching ferritin to an ion channel protein and then tugging the ferritin or heating it with a magnetic field (*Stanley et al., 2015*; *Wheeler et al., 2016*). Here I argue that these claims conflict with basic laws of physics. The discrepancies are large: from 5 to 10 log units. If the reported phenomena do in fact occur, they must have causes entirely different from the ones proposed by the authors. The paramagnetic nature of protein complexes is found to seriously limit their utility for engineering magnetically sensitive cells.

DOI: 10.7554/eLife.17210.001

…”Effect by Ferritin may be due to its paramagnetic properties rather than ferromagnetism…”

Summary

In vivo treatment designed to stimulate the Vagus nerve increases anti-inflammatory CD163-positive monocytes

Modulates mitochondrial membrane potential

In vitro treatment of in vivo activated macrophages
Increases non-opsonized Dynal bead phagocytosis

Open Questions

In vivo treatment of patients with inflammatory diseases?

Modulation of mitochondrial membrane potential in malignant cells?

Does diagmagnetic therapy influence phagosome-lysosome fusion and emperilopoiesis?

Evidence for the contribution of ion channels such as TLRPML-1, TRPM4, Piezo-1?