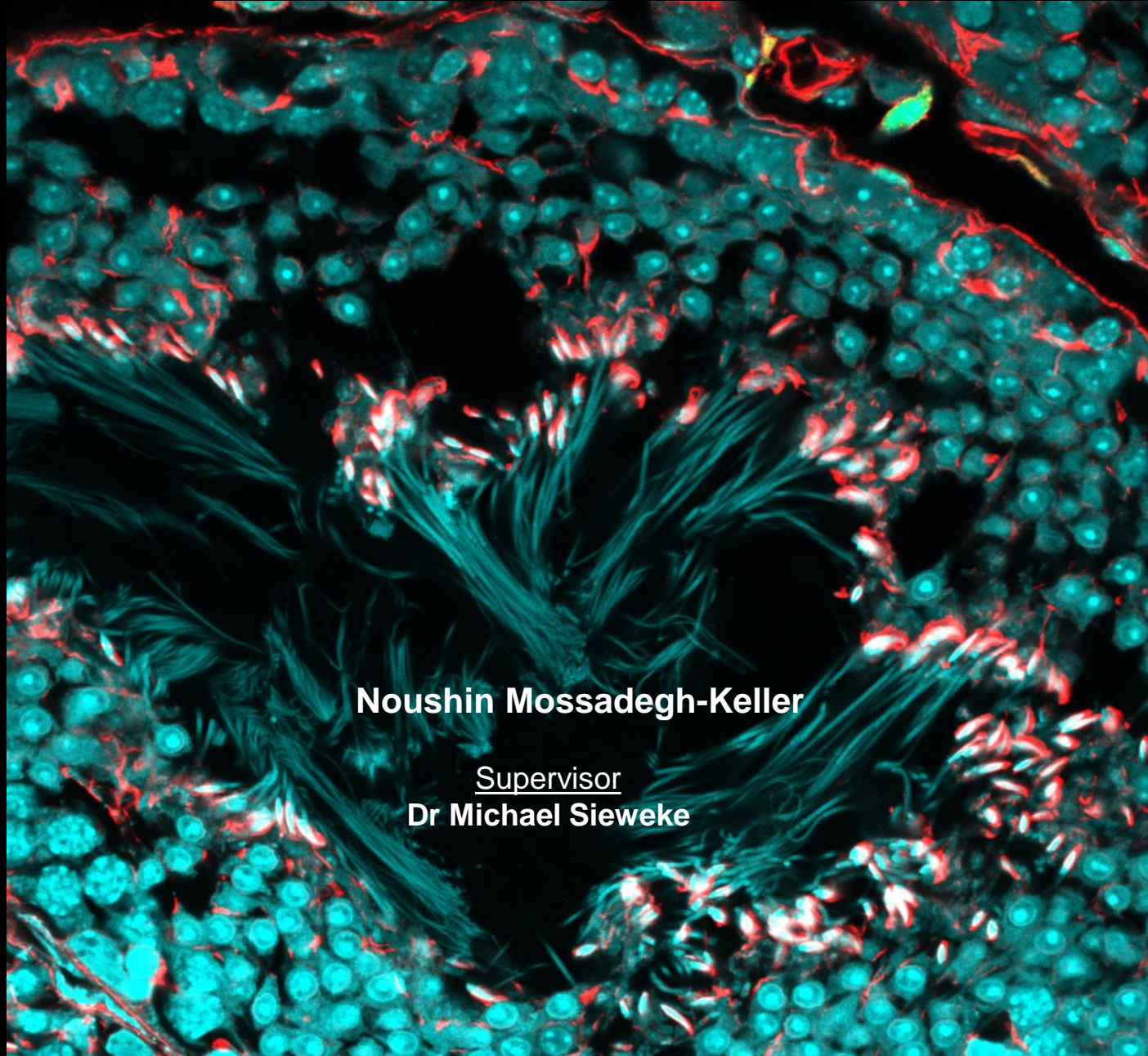


Origin and maintenance of testicular macrophages



Noushin Mossadegh-Keller

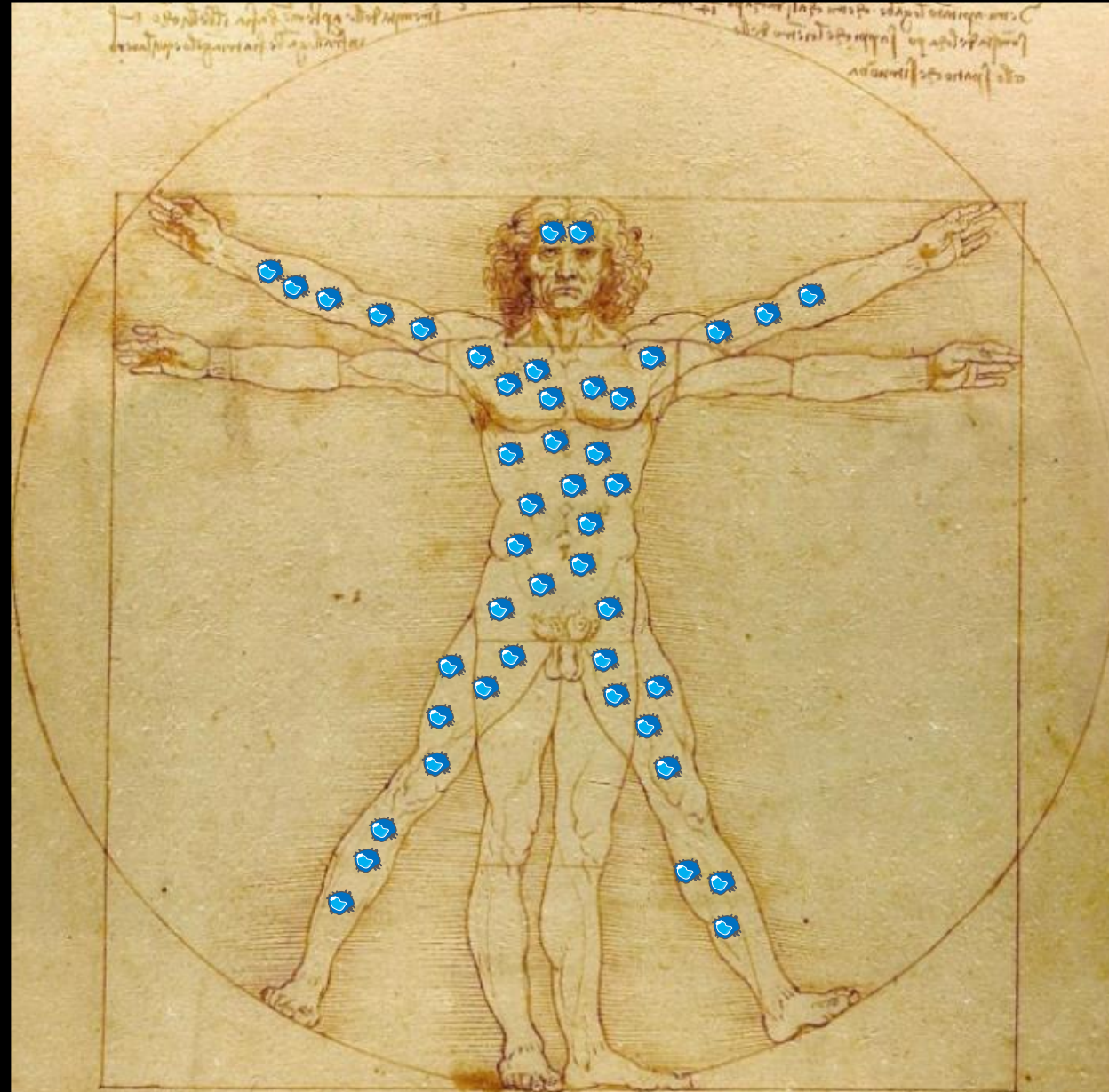
Supervisor

Dr Michael Sieweke

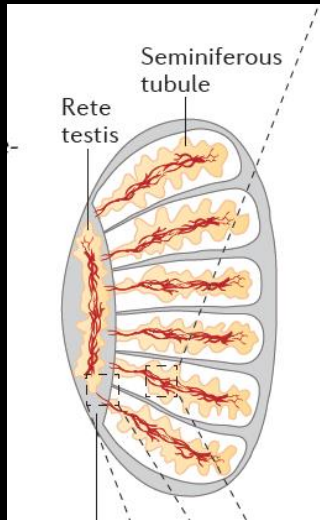
Macrophages: diverse single cell type in the entire body



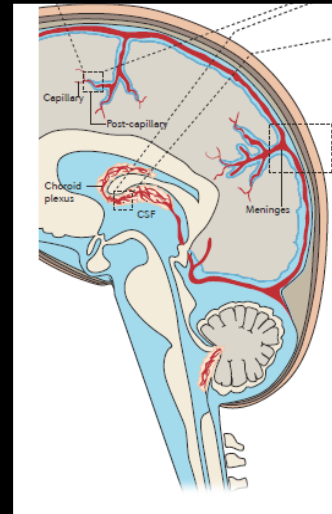
- Immune function
- Trophic function
- Homeostasis/
tissue repair



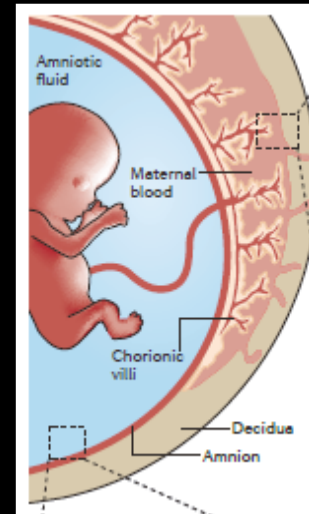
Immunoprivileged organ



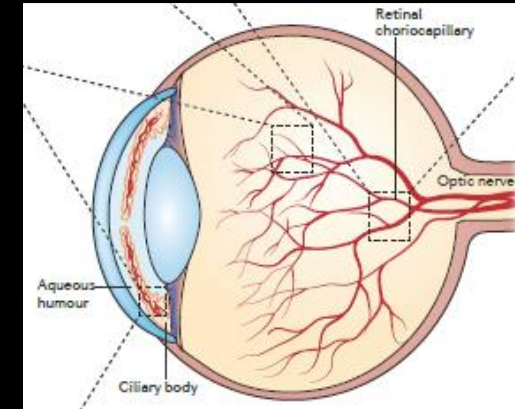
Testis



Brain



Placenta

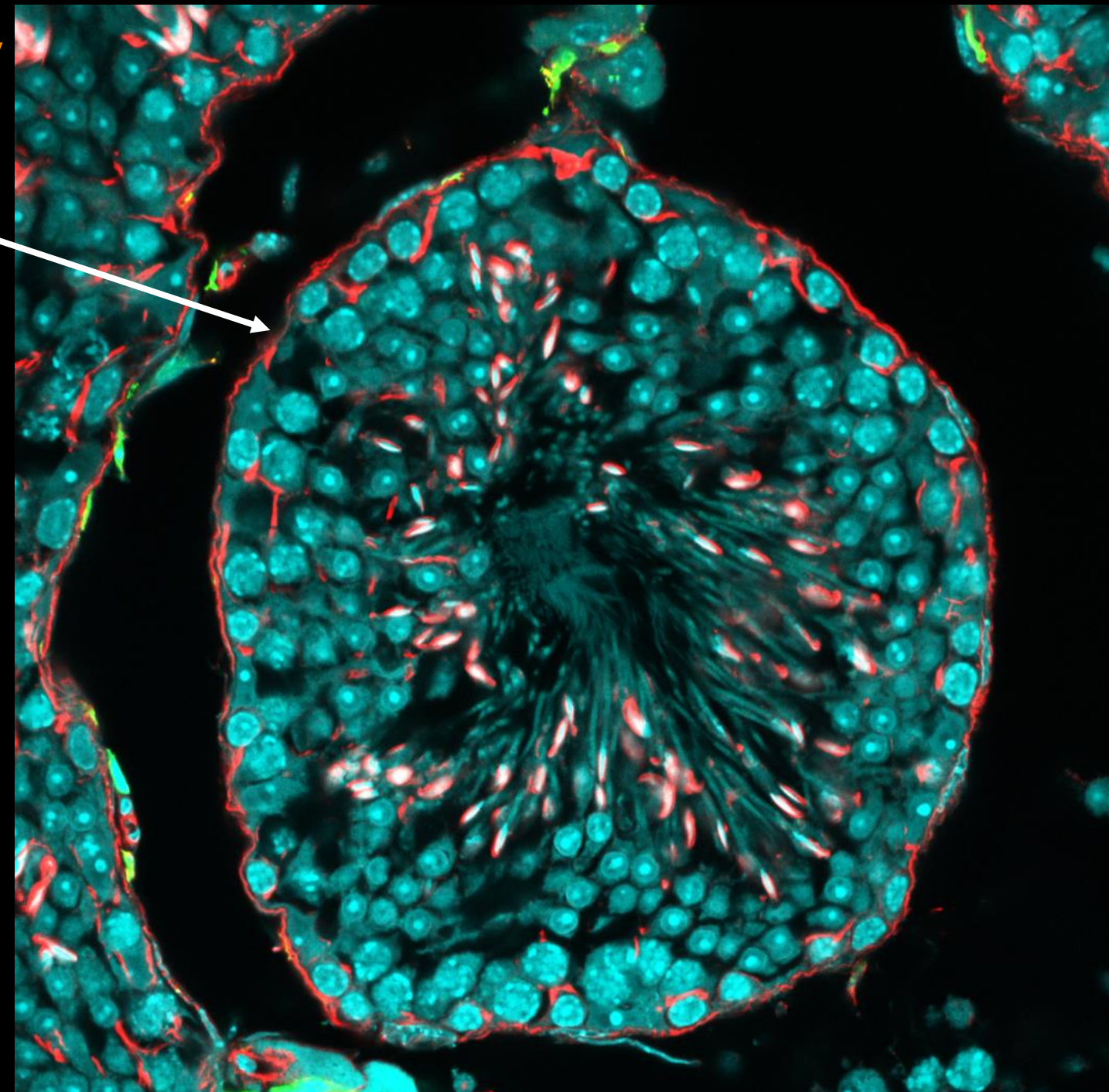
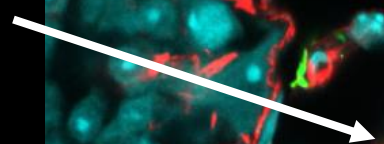


Retina

Absolute barrier to protect those organs from immune cells

Autoimmunity : male infertility

Seminiferous tube



•15% of men infertility

Testicular macrophages

- Macrophages are the most abundant immune cells residing

- Functions:

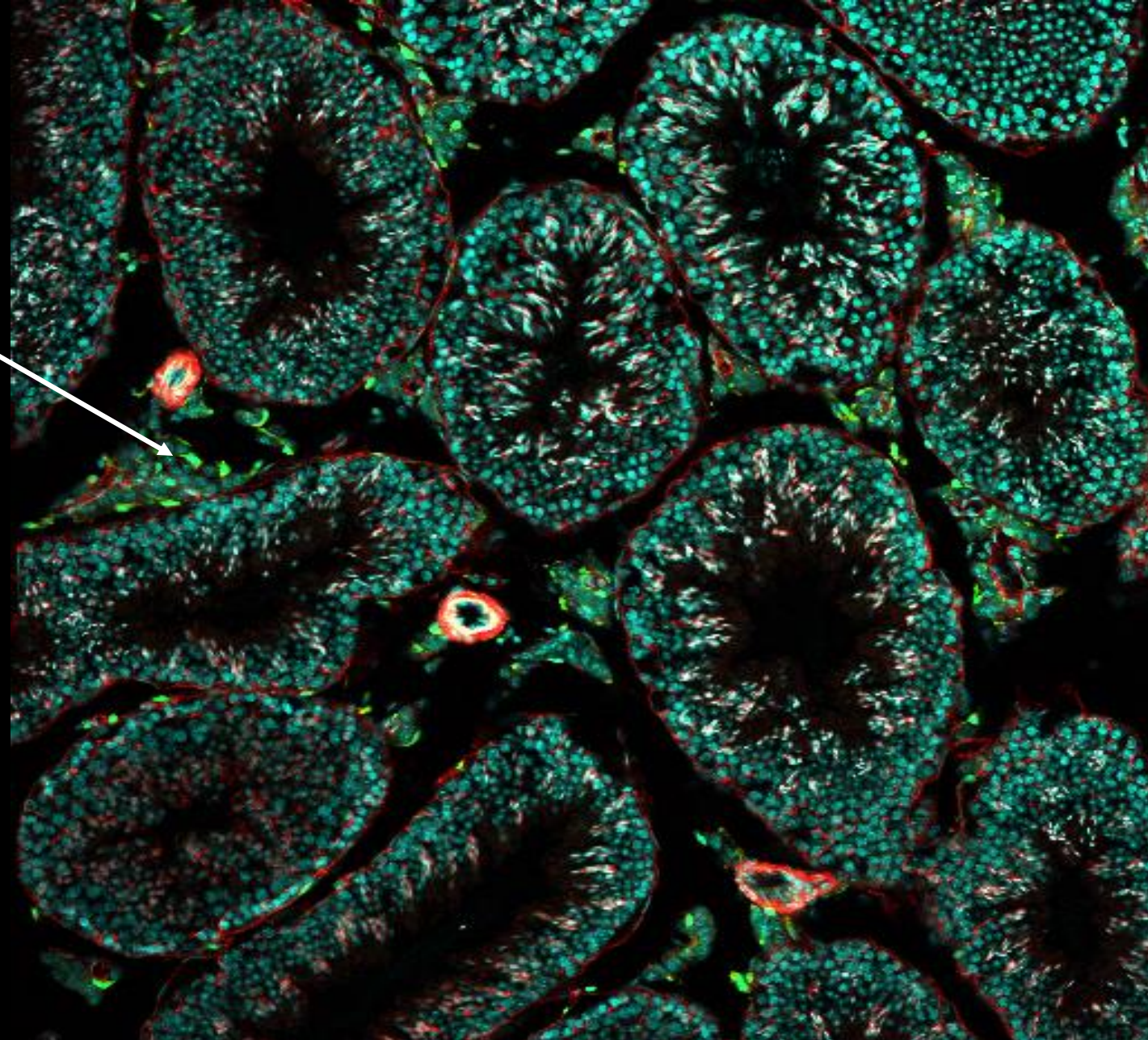
Immunoregulator gate for protecting immunogenic spermatozoa

Defend testis from infection

Trophic on Leydig cell



CX3CR1GFP mice



Ontogeny and maintenance of testicular macrophages

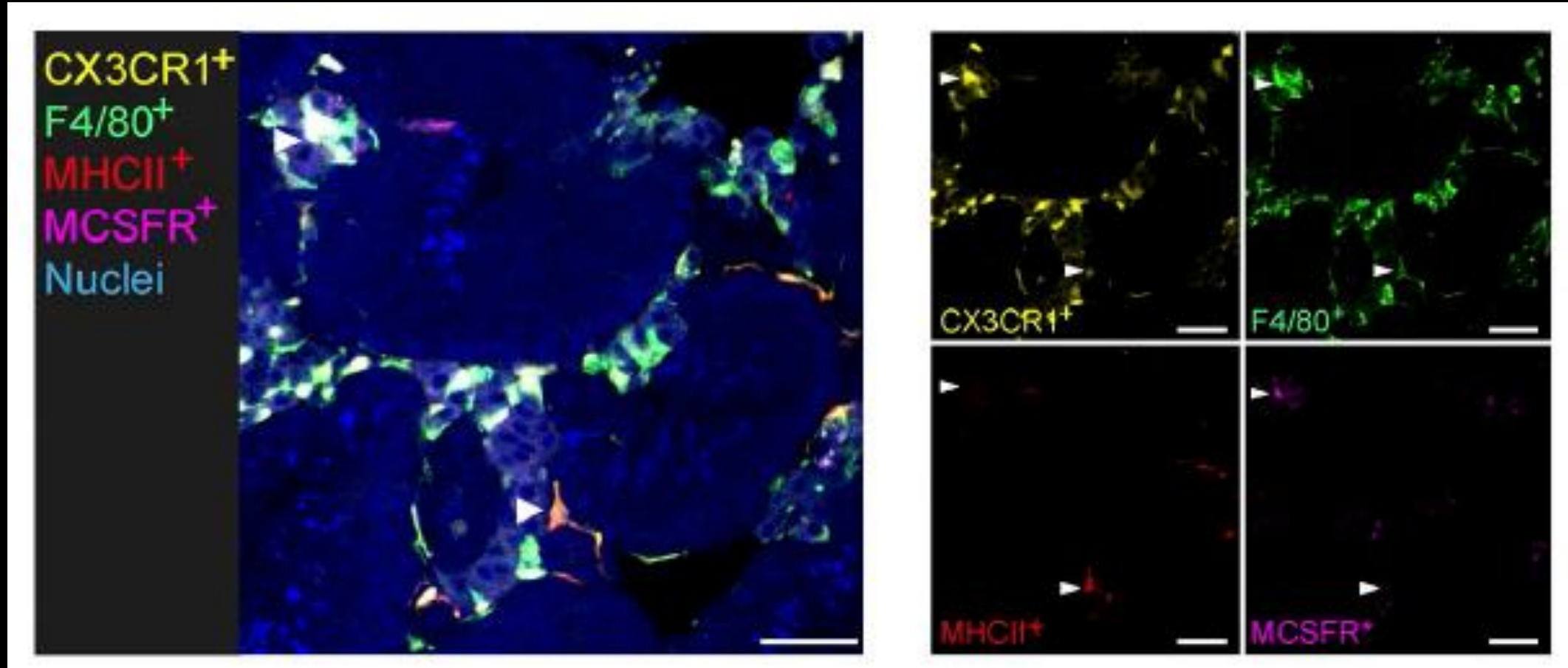
THE JOURNAL OF EXPERIMENTAL MEDICINE

VOLUME 214 NUMBER 10 OCTOBER 2017 www.jem.org



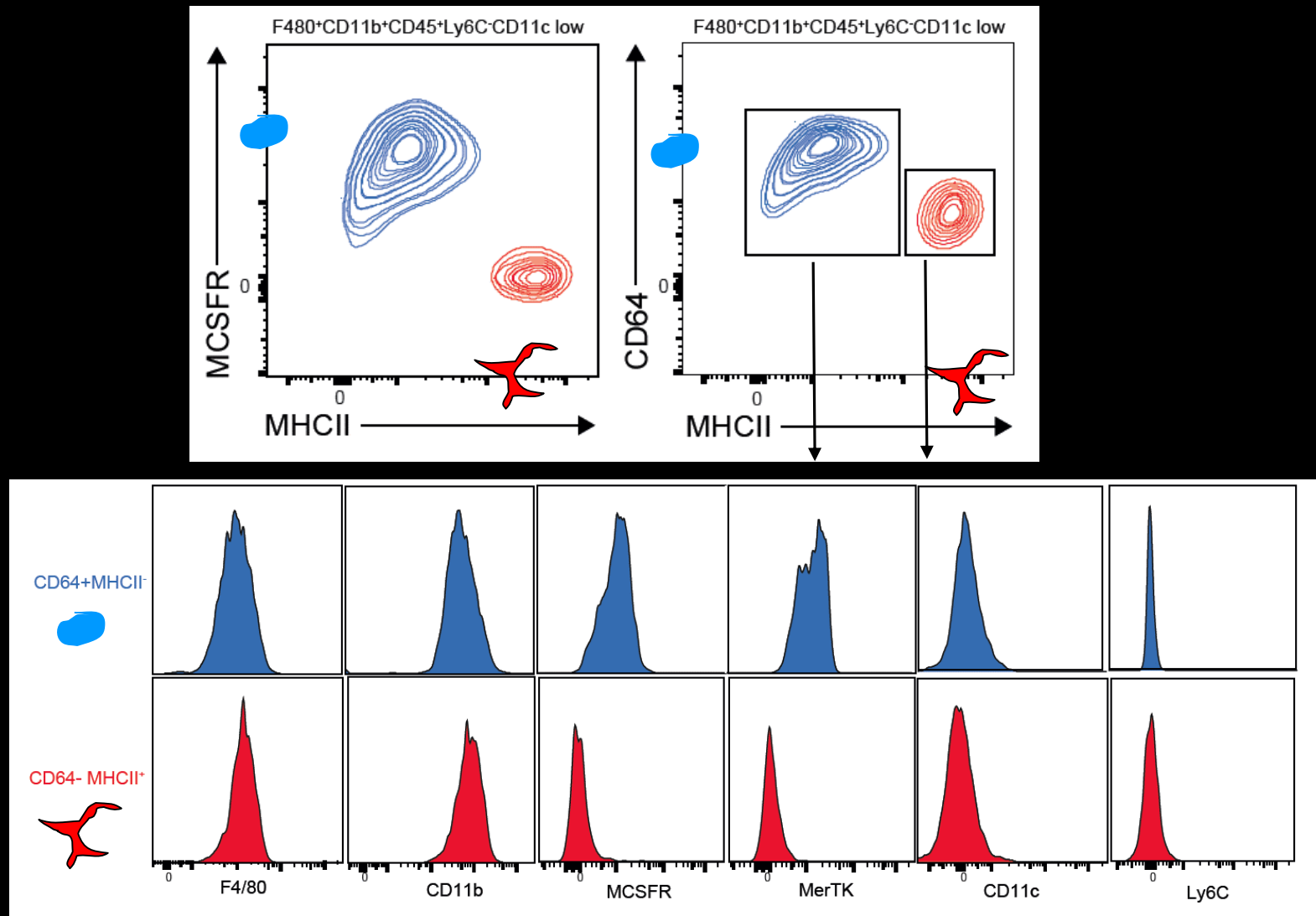
ORIGIN OF TESTICULAR MACROPHAGES
Brain Cancer Defeated by Zika Virus
Osteocalcin Corrects Cognitive Decline

Characterization of TestisMAC populations



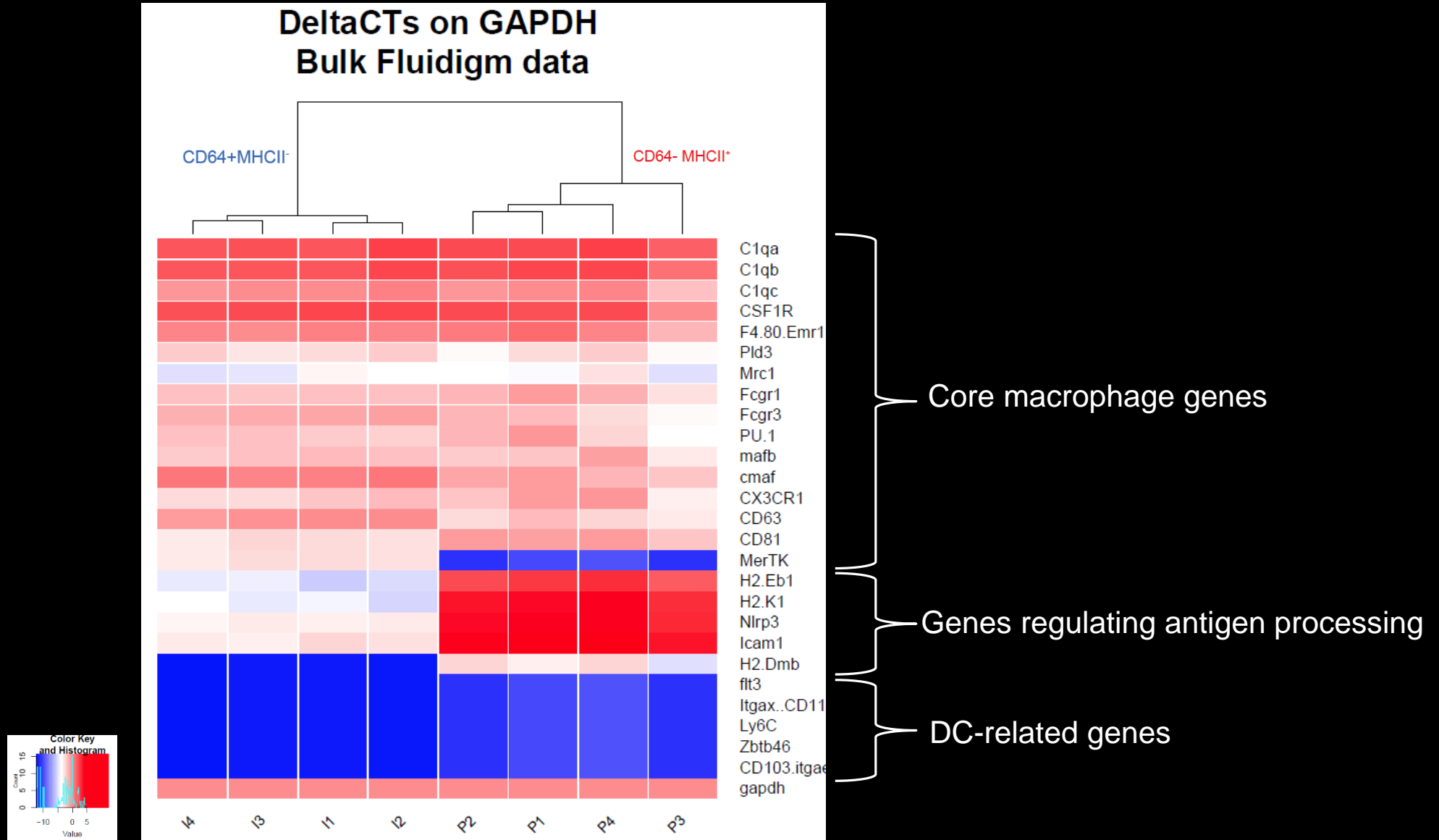
Heterogeneity of Testicular macrophage populations: interstitial MAC and peritubular MAC

Characterization of TestisMAC populations



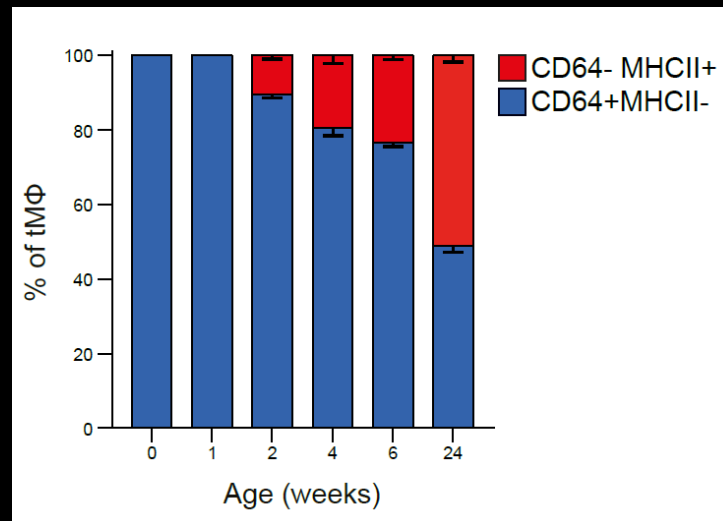
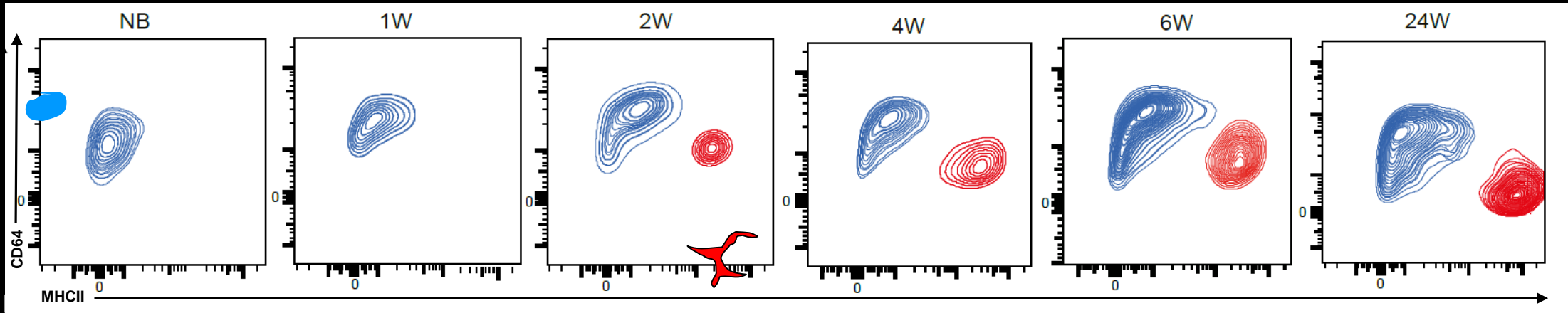
Characterization of the two testisMAC populations by cell surface marker

Characterization of TestisMAC populations



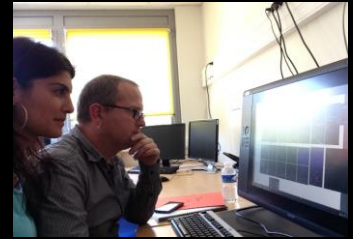
Characterization of the two testisMAC populations by gene expression profiling

Postnatal development of TestisMAC populations

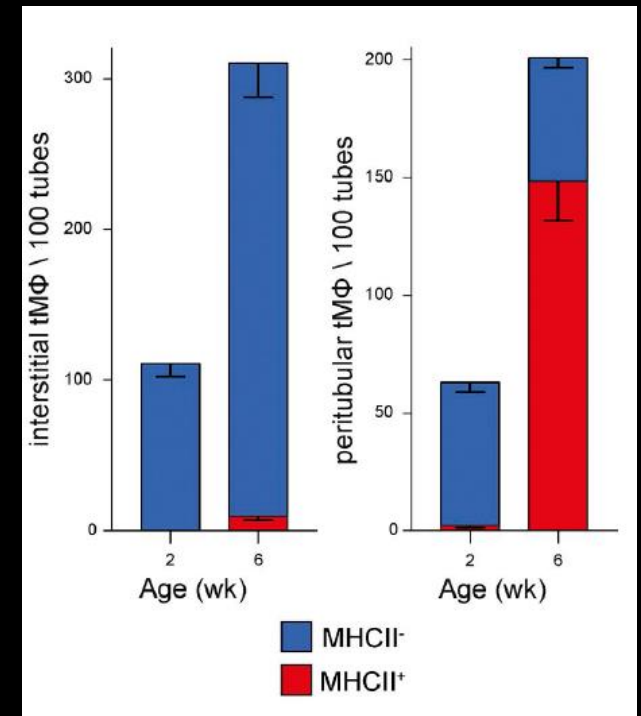
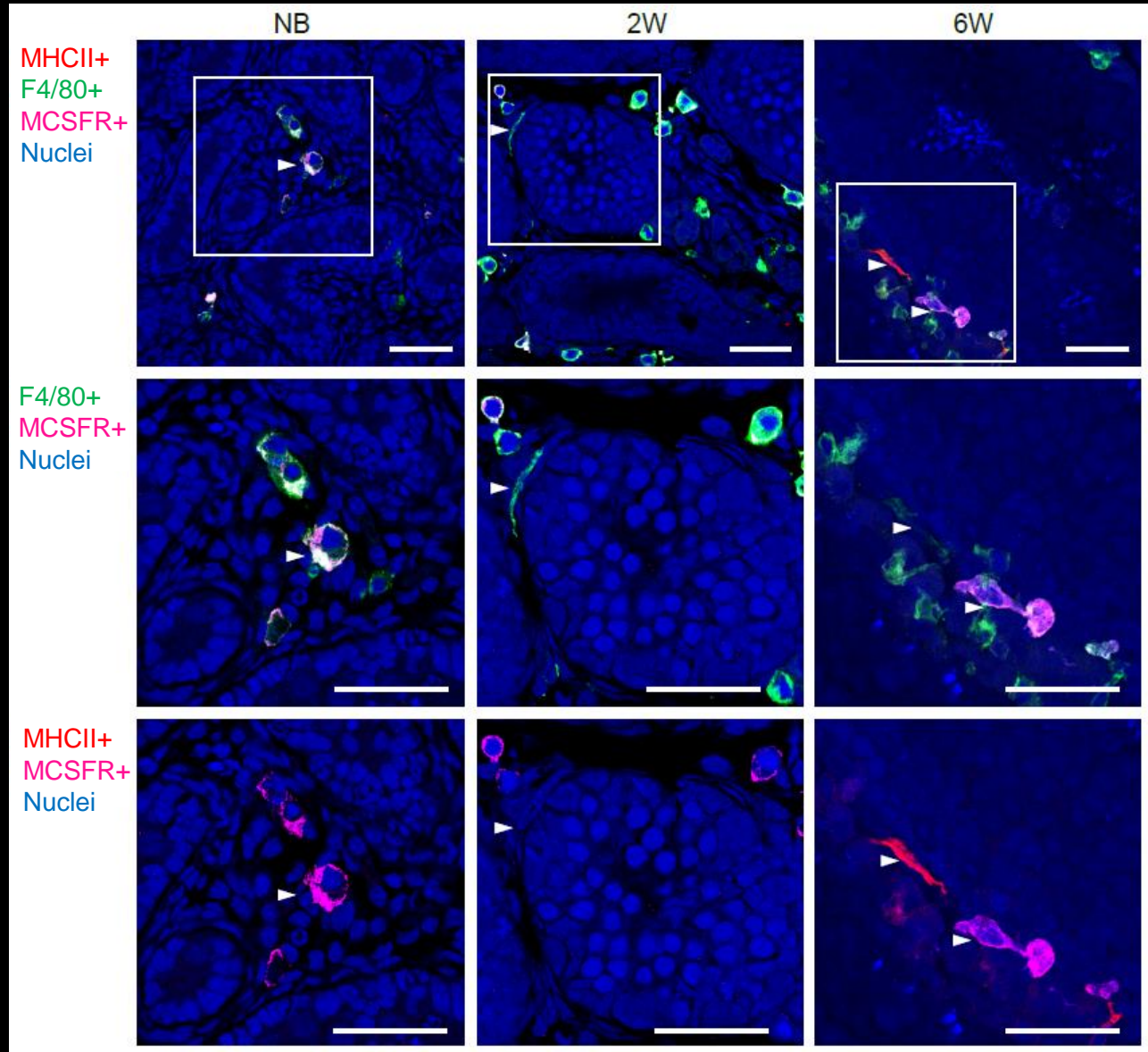


Interstitial population already presents at birth but peritubular population emerges 2w after !

Postnatal development of TestisMAC populations



S. Mailfert



Interstitial population already presents at birth but peritubular population emerges 2w after !

Characterization of two testisMAC populations during postnatal dvt

1. Identification of these two populations by cell surface markers and gene expression profiling
2. Kinetics of these 2 populations during postnatal development

2 populations TestisMAC with different :

- morphology
- localization
- marker
- kinetics of emergence

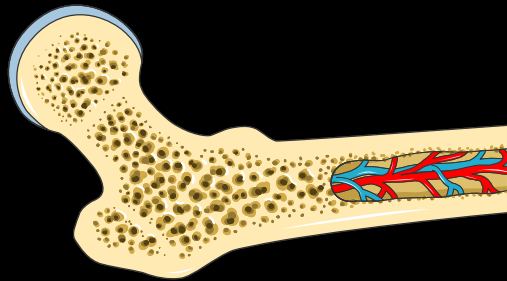


Origin and self maintenance of tissue resident macrophages

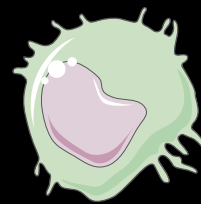


**Embryonic
progenitor**

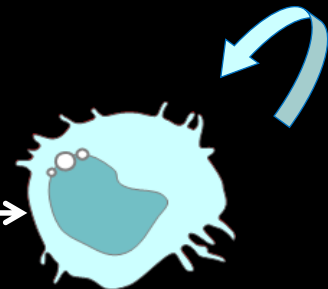
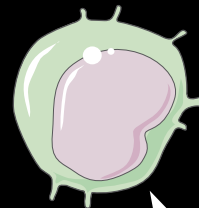
Ginhoux et al. Science 2010
Schulz et al. Science 2012
Hoeffel et al. JEM 2012
Yona et al. Immunity 2013
Hashimoto et al. Immunity 2013
Tamounoudour et al. Immunity 2013
Epelman et al Immunity 2013
Molawi et al. JEM 2014
Bain and al Nature Immunology 2014



**BM
progenitor**

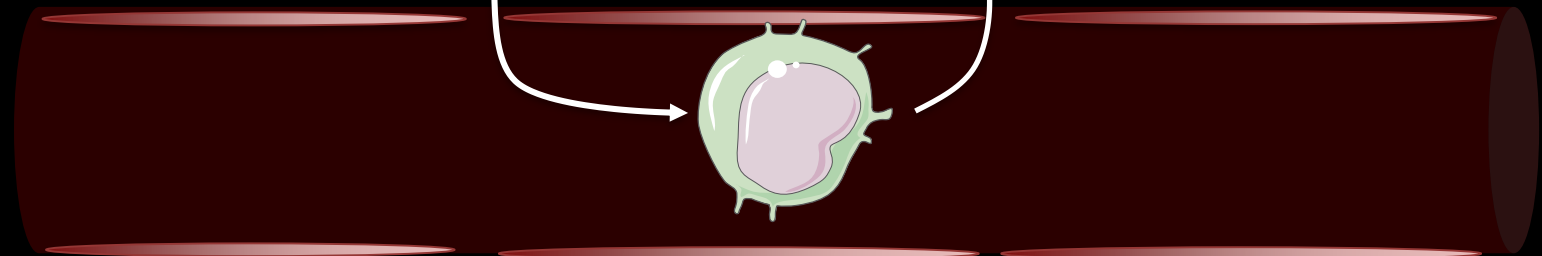


short-lived
recruited MNP

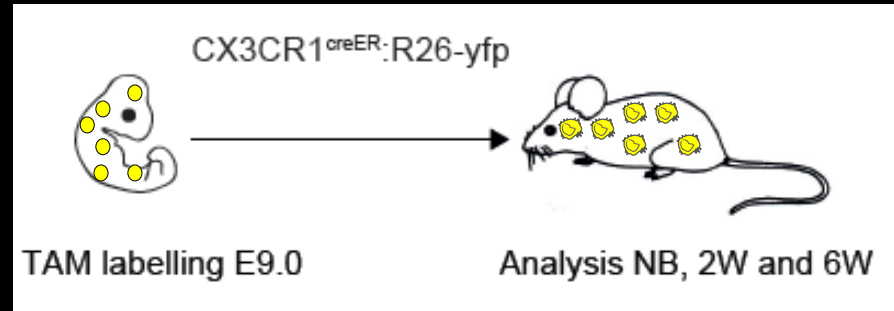


MHCII⁺

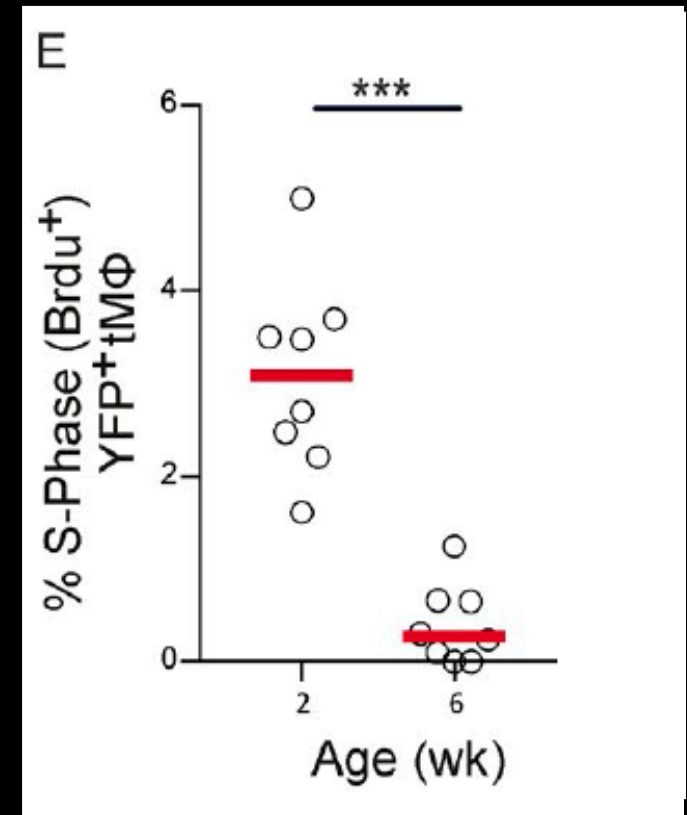
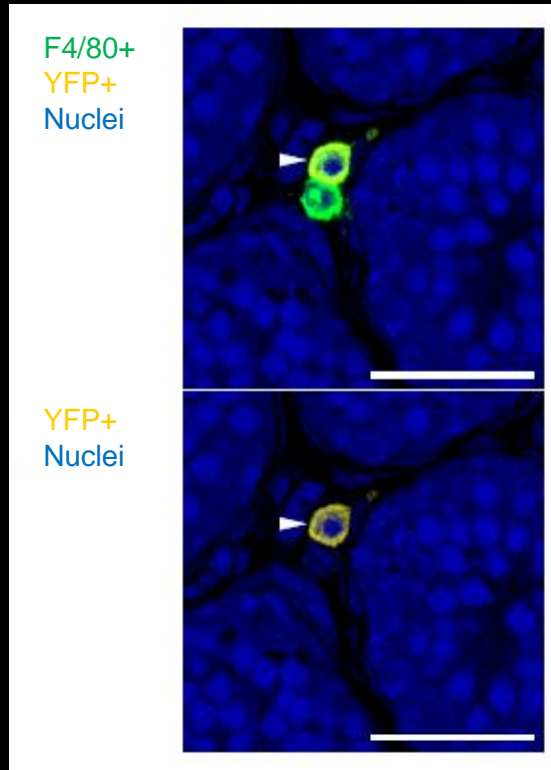
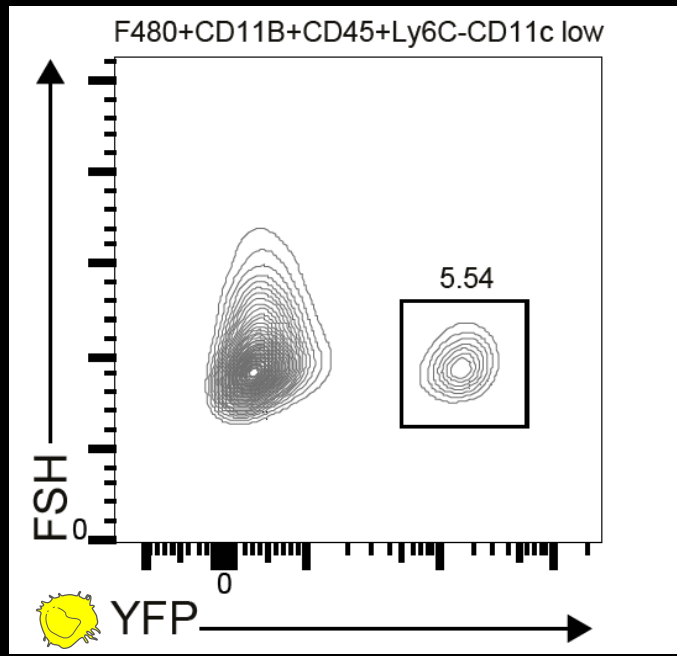
MHCII⁻
Tissue
resident
macrophage



Origin of testisMAC: embryonic?

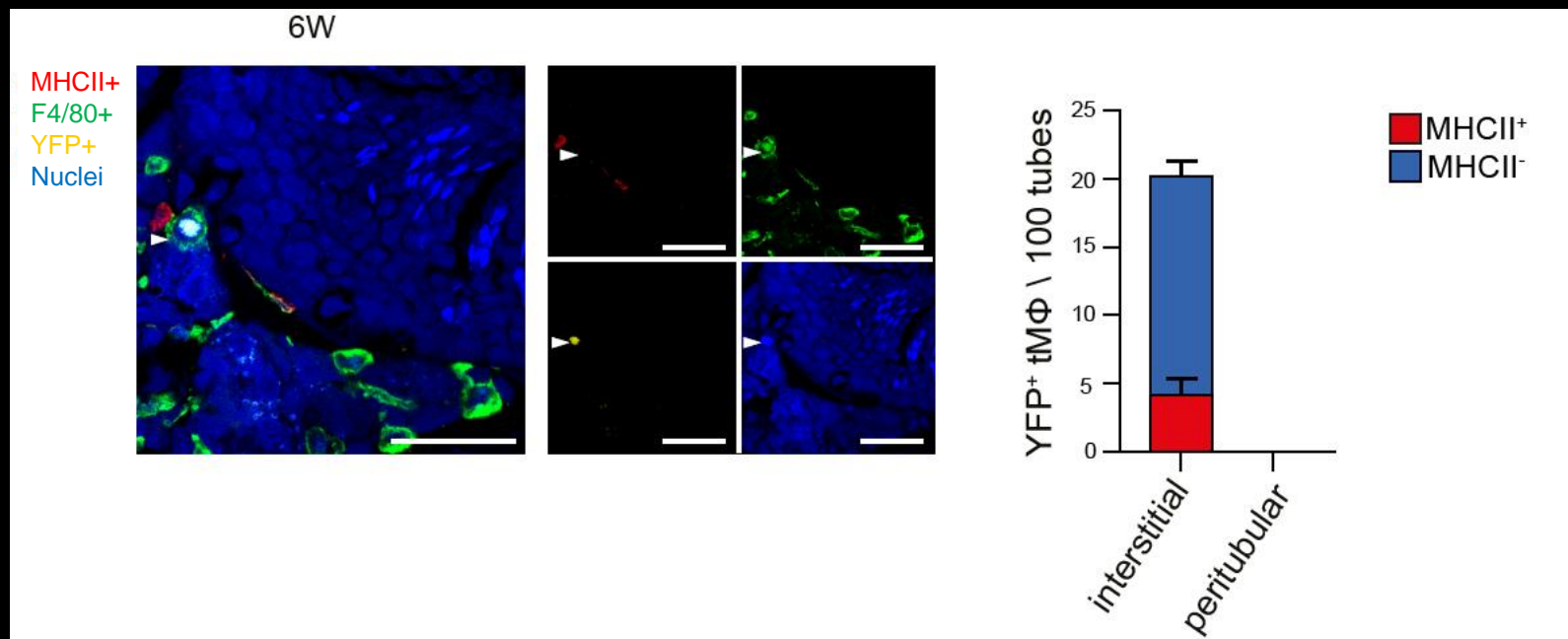
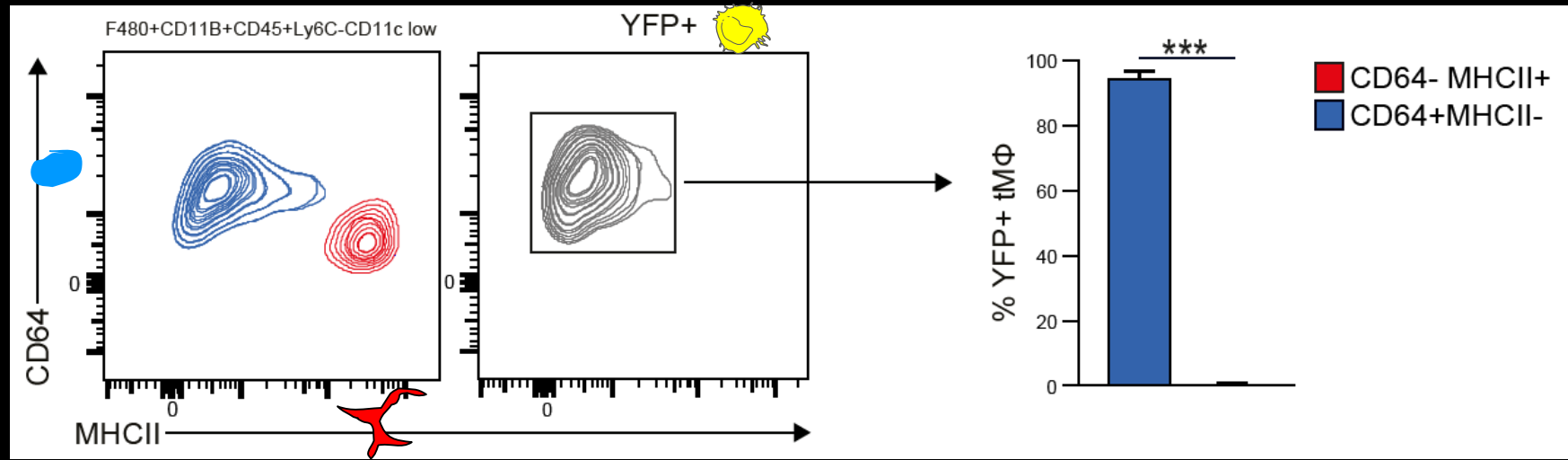


Lineage traced YFP + cells
in newborn testes



Contribution of embryonic macrophages in the mice testis

Origin of testisMAC : embryonic?



Embryonic macrophages contribute exclusively to interstitial population

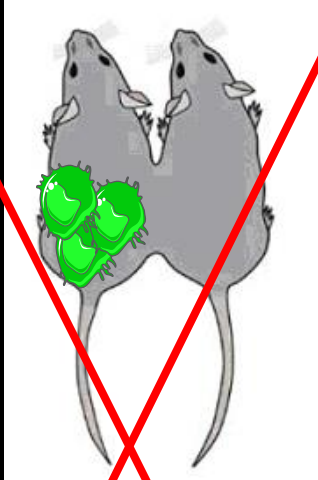
Embryonic macrophages contribute to interstitial population

1. Embryonic derived MAC give rise exclusively to interstitial TestisMAC
2. Where are the peritubularMAC? Other origin?

Origin of peritubular MAC: bone marrow?

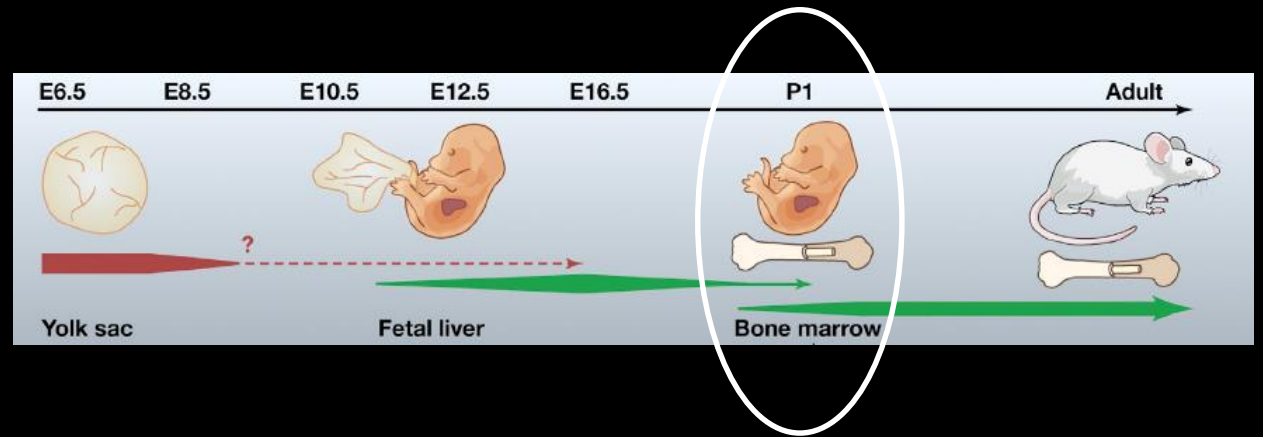
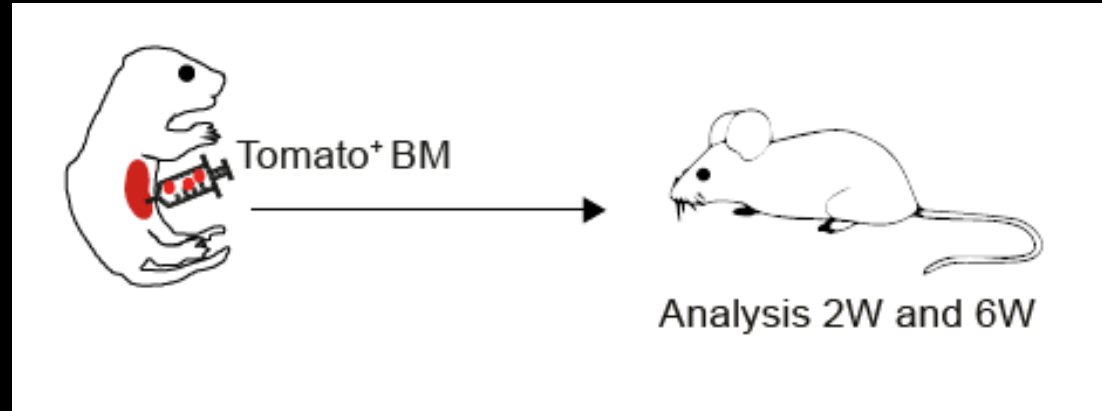


Parabiosis



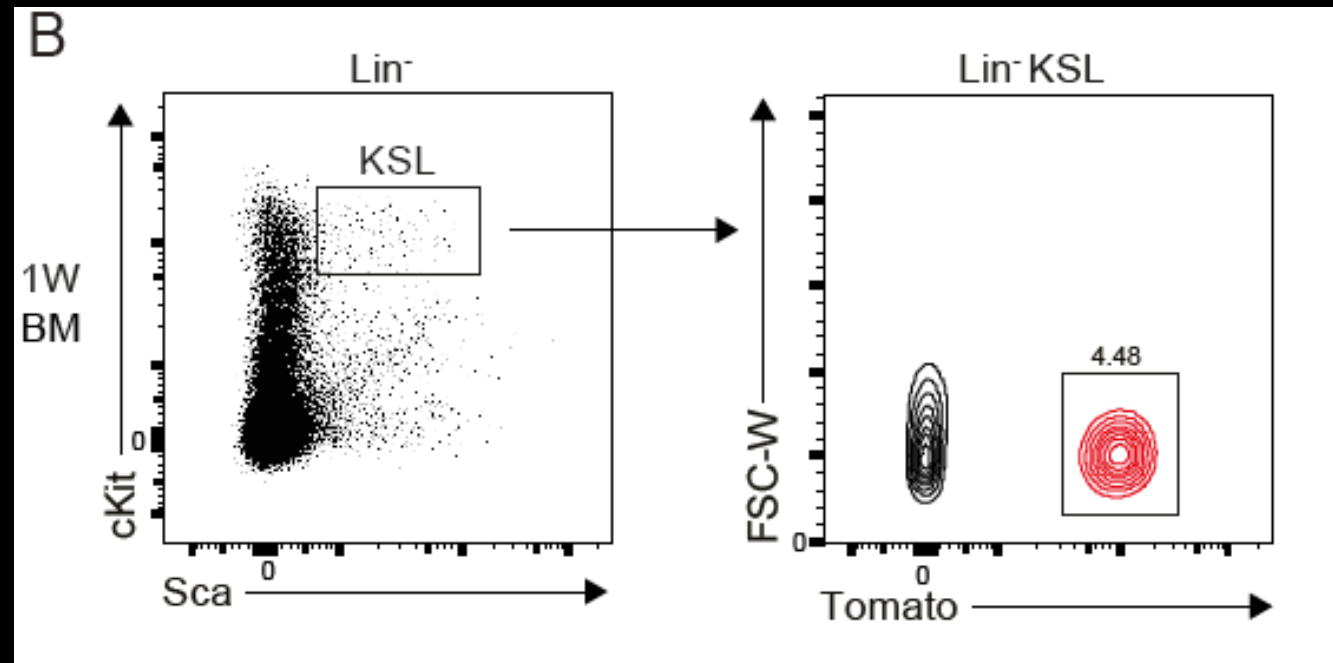
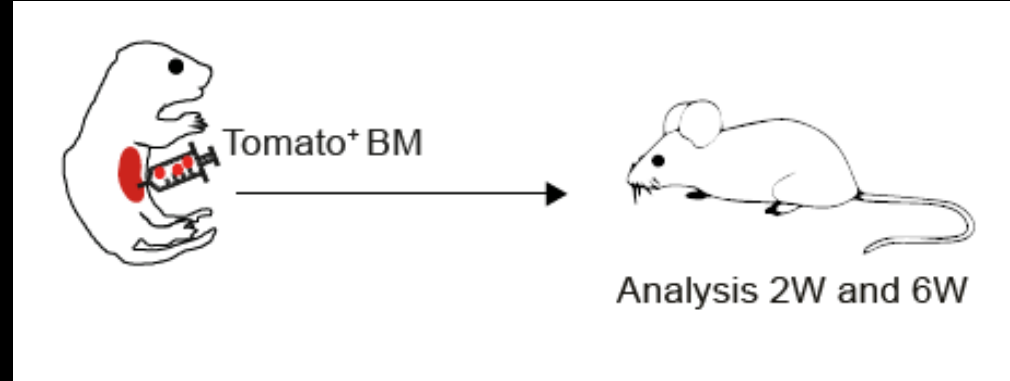
CX3CR1-GFP x WT

Chimera



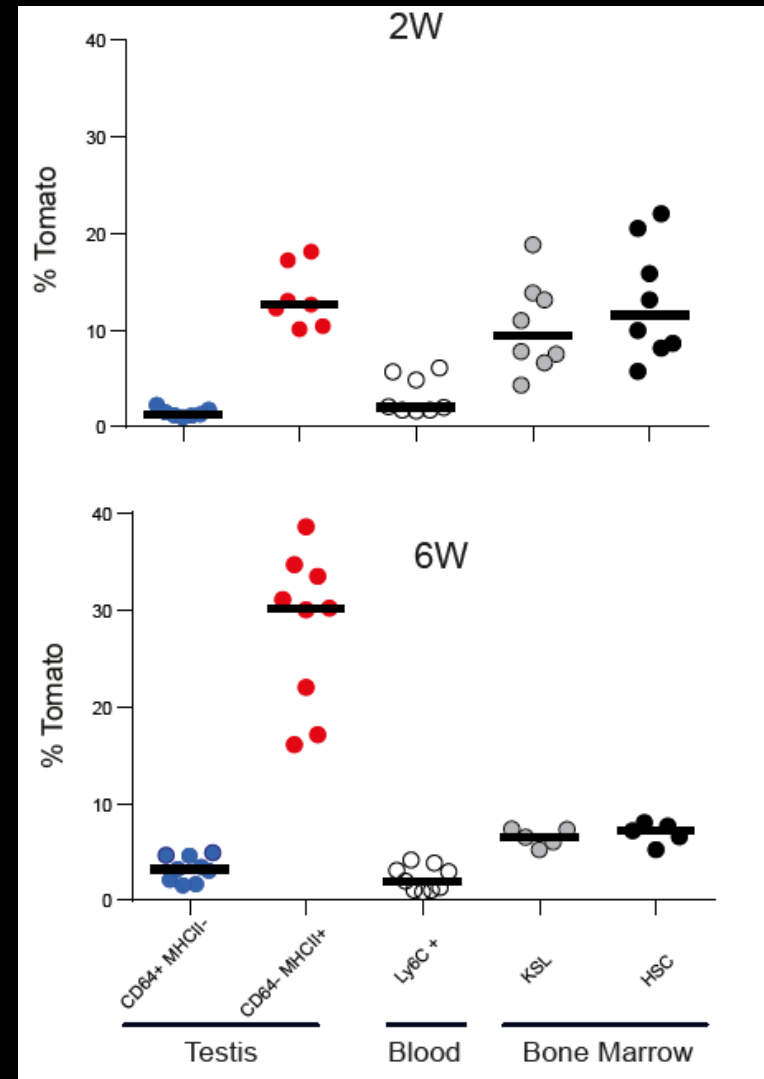
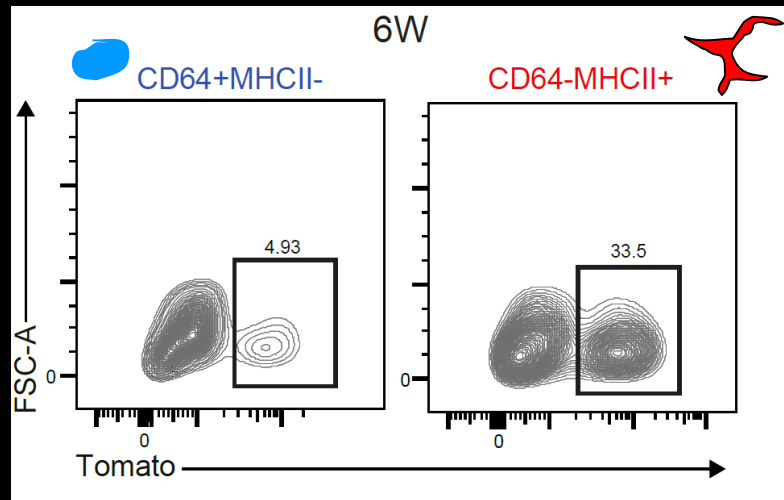
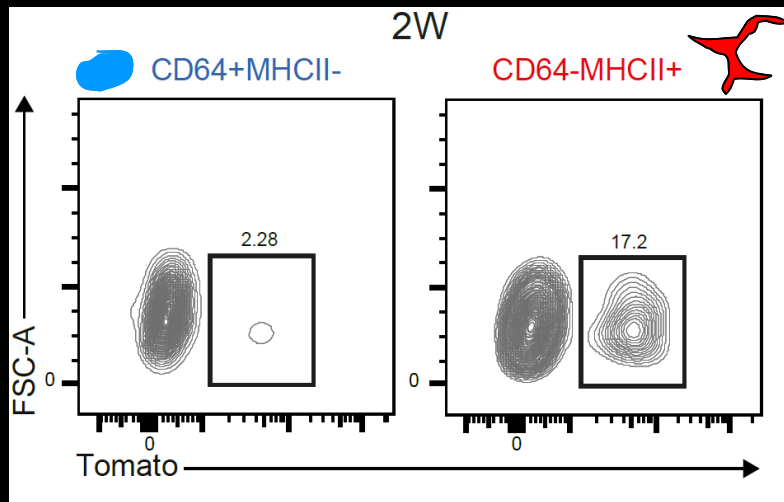
Adapted from Epelman and al, Immunity 2014

Origin of peritubularMAC: bone marrow?



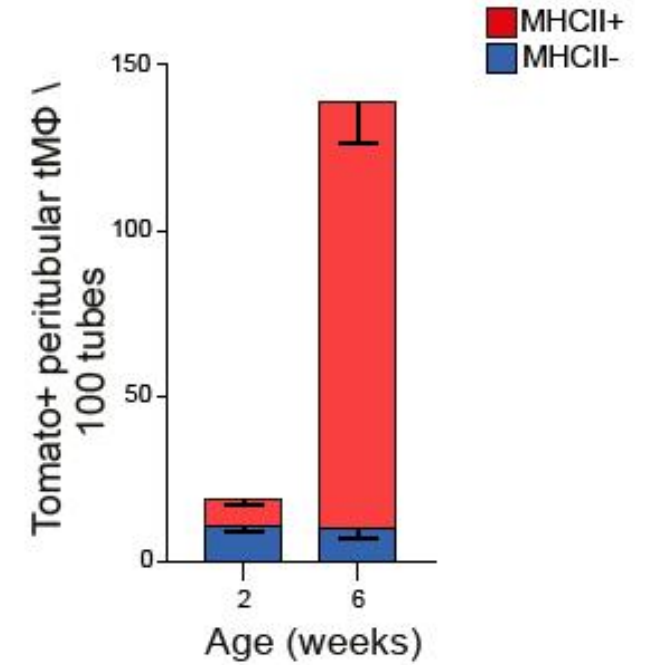
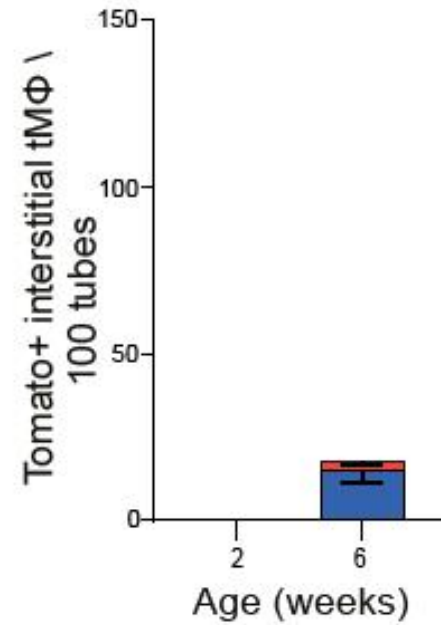
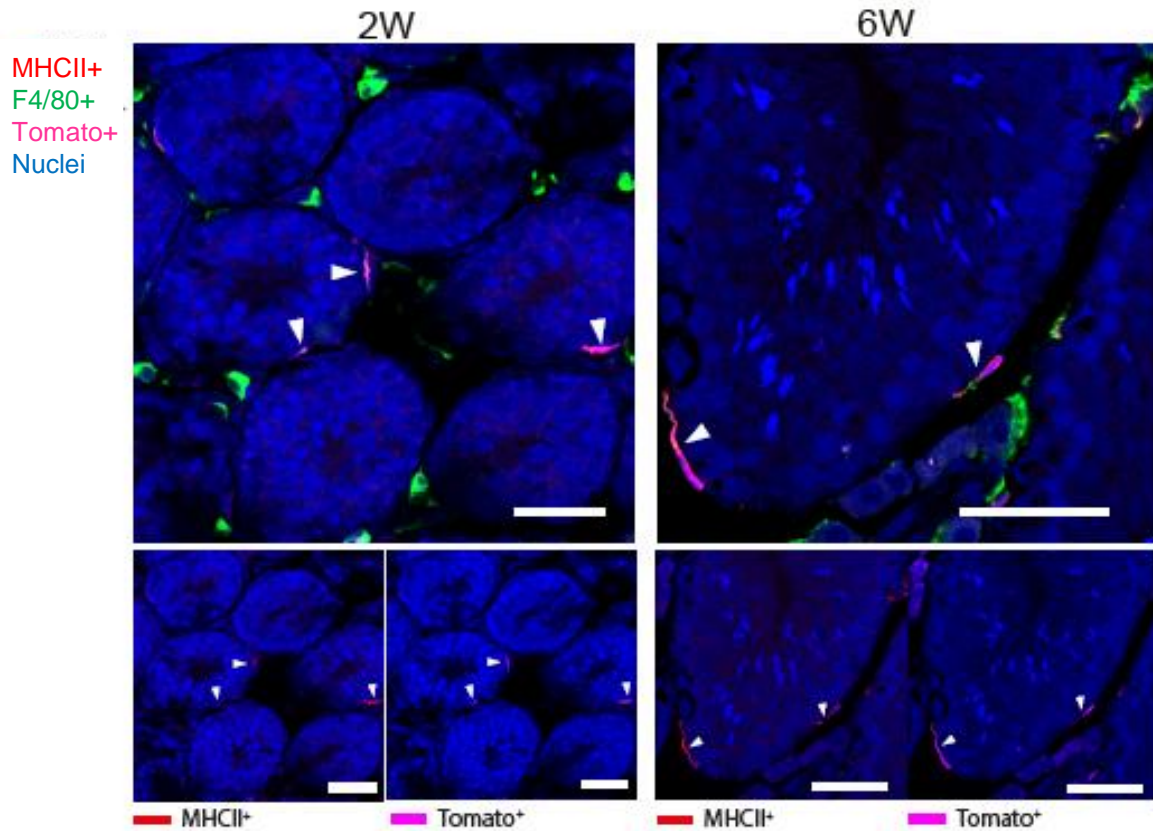
Validation of the lineage tracing model: HSCs reach the BM one week post-transplant.

Origin of peritubularMAC: bone marrow?



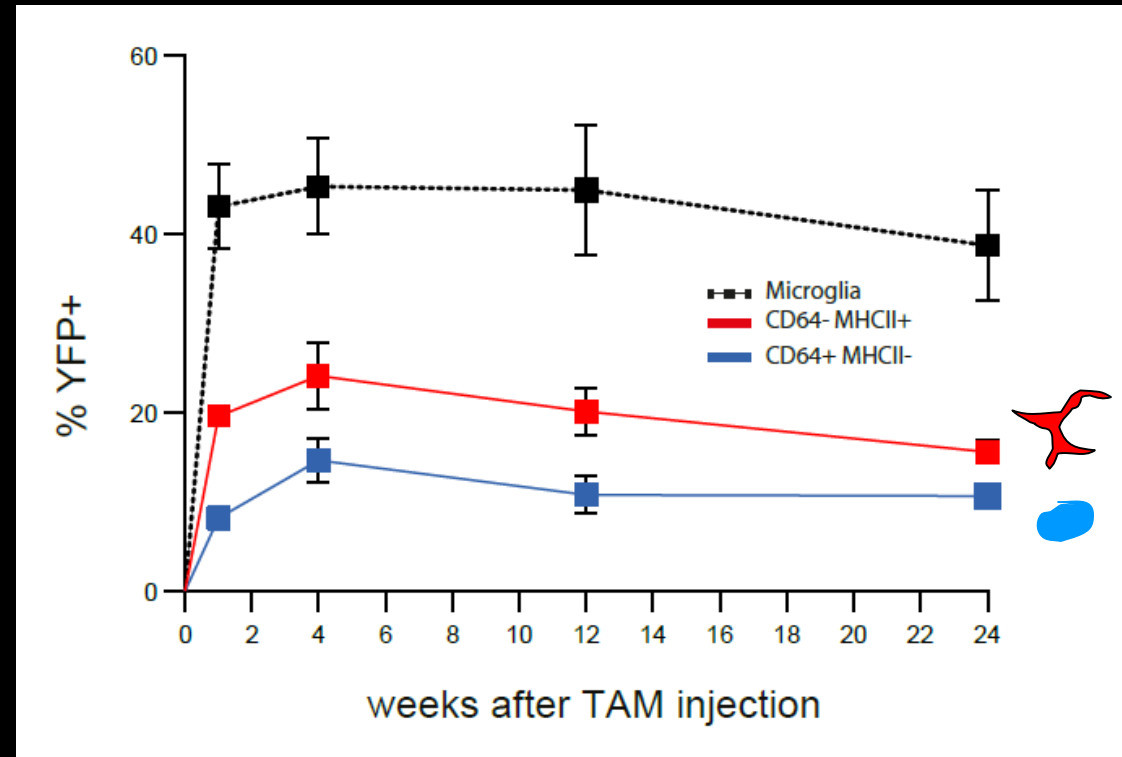
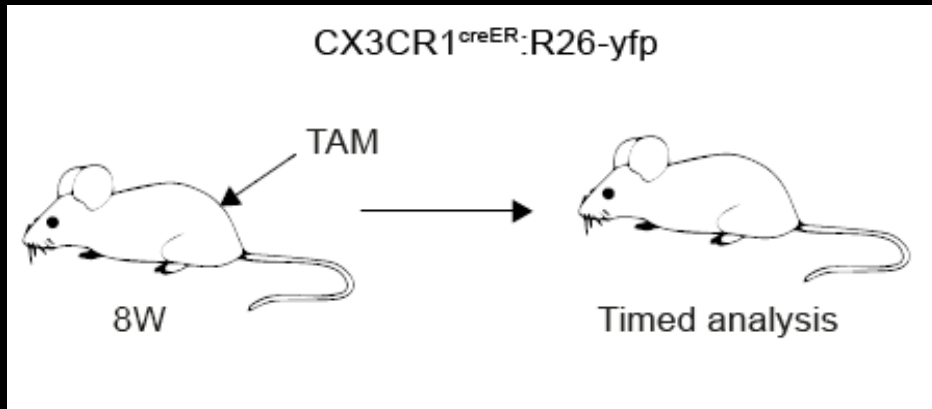
PeritubularMACs derive from BM progenitors

Origin of peritubular MAC: bone marrow?



Peritubular MAC derive from BM progenitor

Lifespan: long-lived or constantly replenished?



TestisMACs are long-lived !

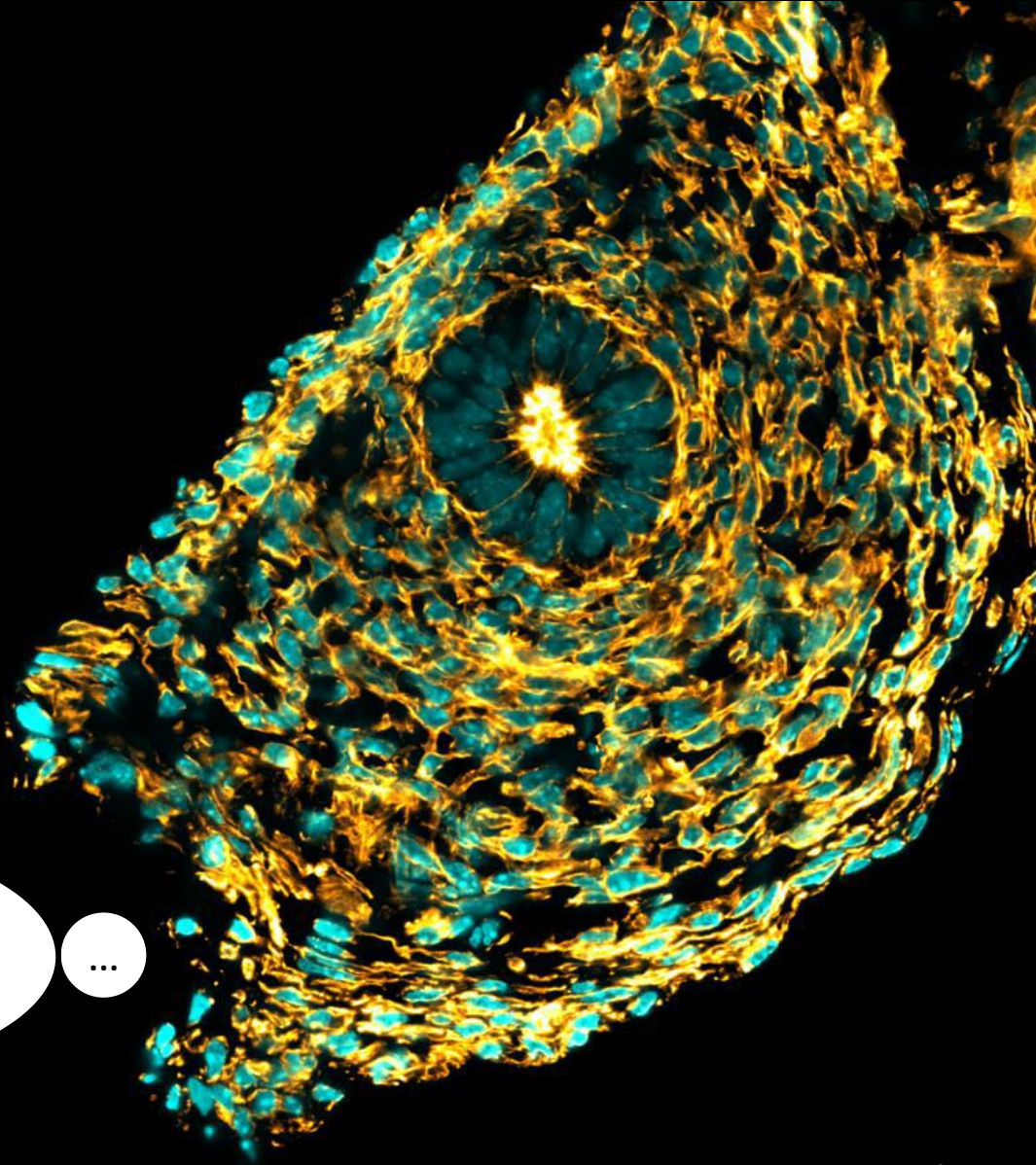
Perspectives

Implication of each
testisMac population in the
role of guardian of fertility ?

Could origin dictate
macrophage functions?

Does ontogeny
matter ?

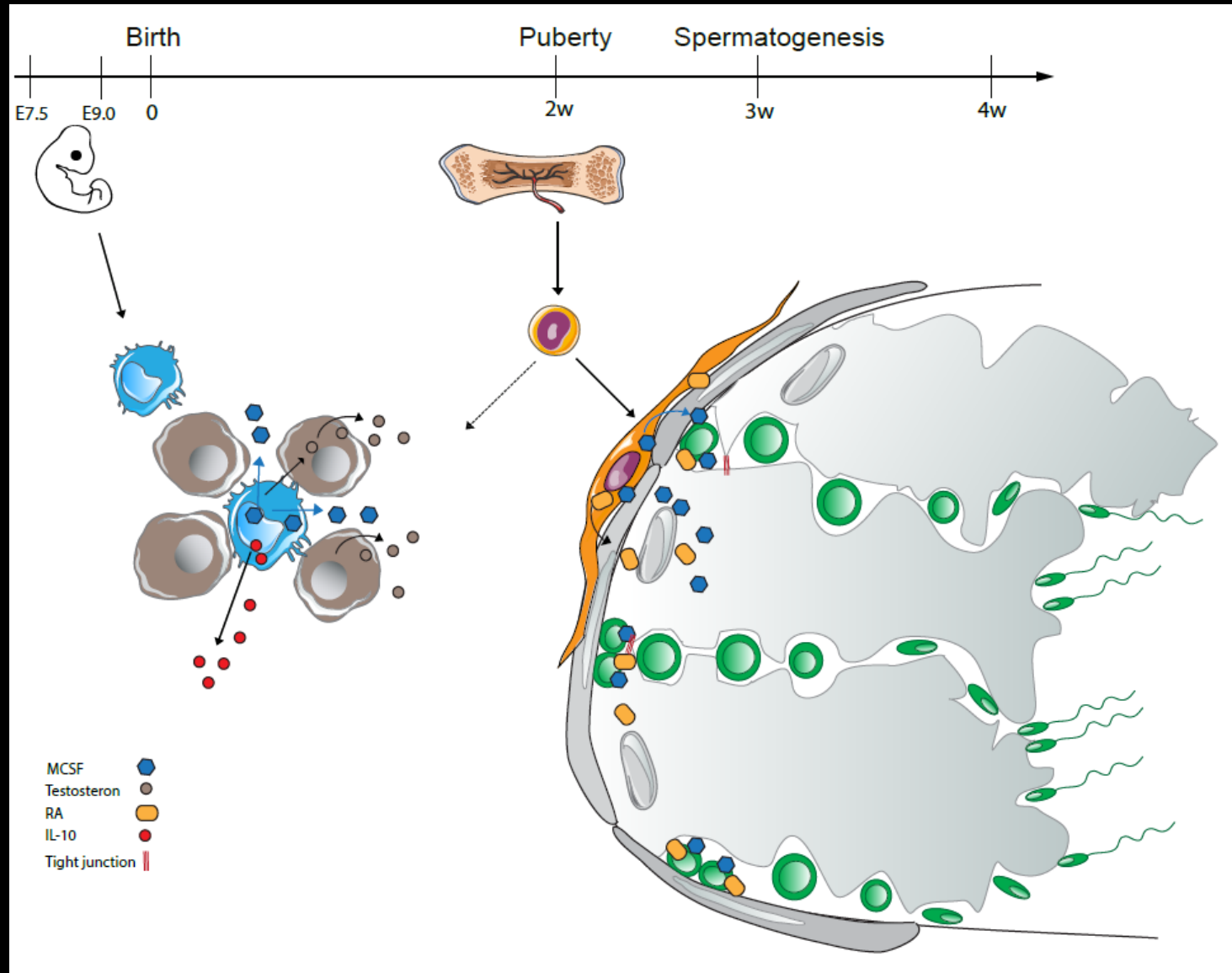
...



This is not a St Pierre fish but a testis...

First price of the France-Bioluminescence contest
Second price contest INSERM 50 ans

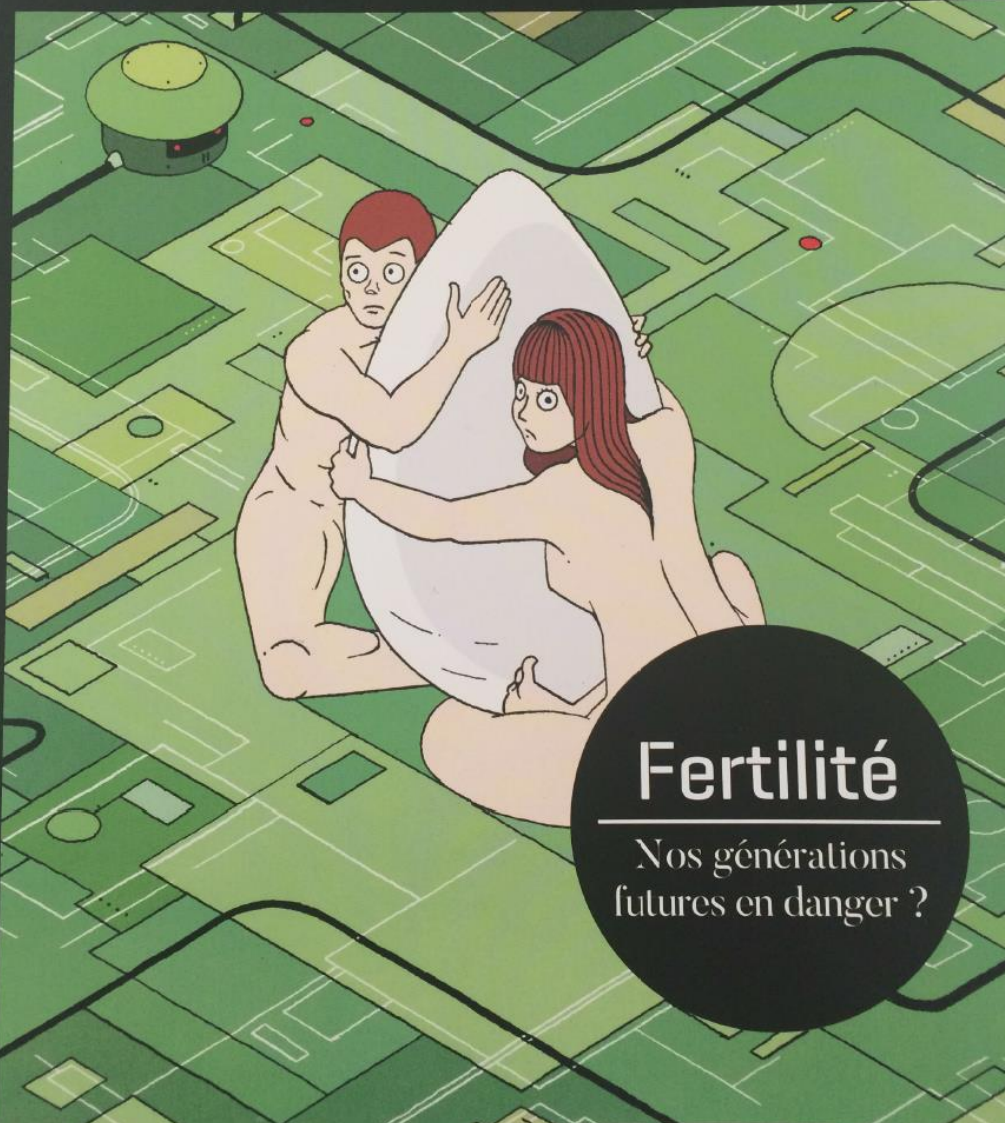
Testicular macrophages: guardians of fertility



Science & santé

LE MAGAZINE DE L'INSTITUT NATIONAL
DE LA SANTÉ ET DE LA RECHERCHE MÉDICALE

Maladies rares
Orphanet fête ses 20 ans
Institut clinique de la souris
Des moustaches à la queue
La recherche publique française
Toujours attractive ?



Fertilité

Nos générations
futures en danger ?

36

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JUIN 2017

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Acknowledgements



TestisTeam / Collaborators



R. Gentek

M. Bajenoff

Cytometry facility

S. Bigot



Imaging facility

S. Mailfert



Animalhouse facility

L. Razafindramanana

Thanks for your attention

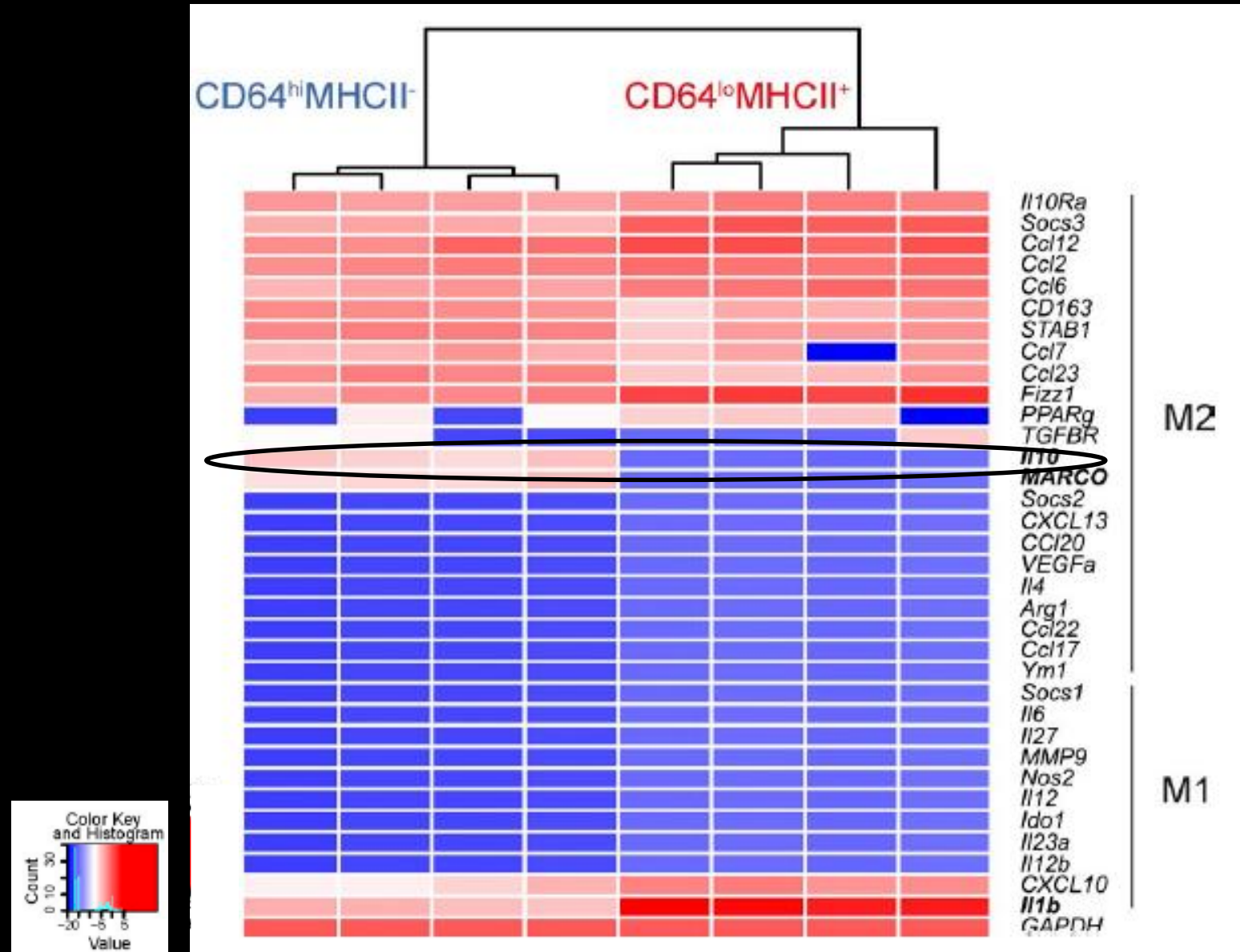


PHILIPPE DE LORENZO
L'ART ET LA SCIENCE

Artiste et scientifique de renom, Philippe de Lorenzo explore les liens entre l'art et la science à travers ses œuvres. Ses créations sont inspirées par les découvertes scientifiques et les avancées technologiques. Son travail est une véritable exploration de la beauté et de la complexité du monde qui nous entoure.



Characterization of TestisMAC populations



Characterization of the two testisMAC populations by gene expression profiling