



Insights into prepartum cervix remodeling and approaches from LLUSM resources

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CENTER FOR PERINATAL BIOLOGY

Loma Linda University School of Medicine

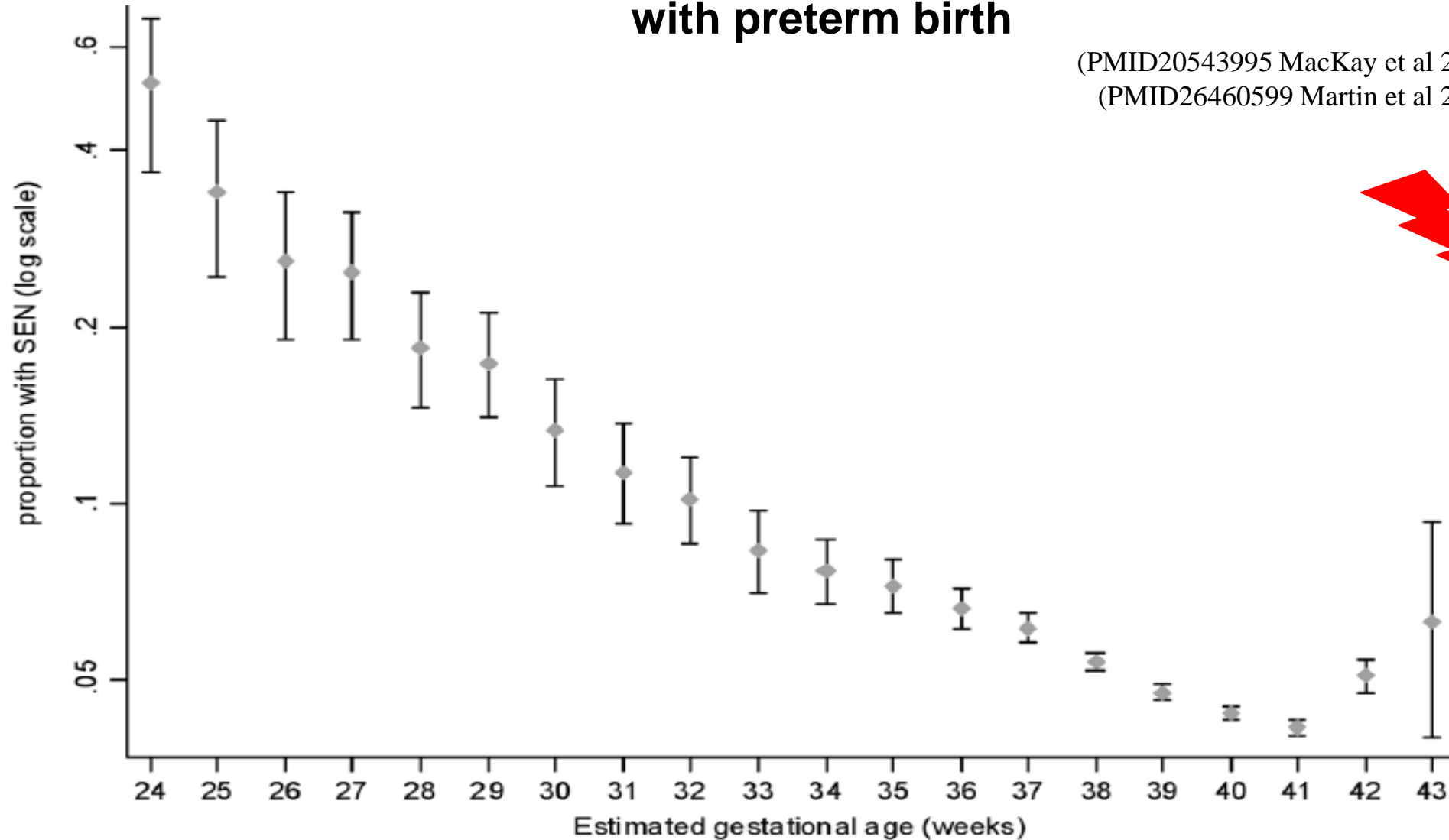
Director of Infrastructure and Core Facilities

October 21, 2016 LLU Basic Sciences Symposium

PTB 2012 World health report and 2014 NCHS-USA

Increased special education needs with preterm birth

(PMID20543995 MacKay et al 2010)
(PMID26460599 Martin et al 2014)



10 countries
account for 60% of
the world's preterm
births by rank:

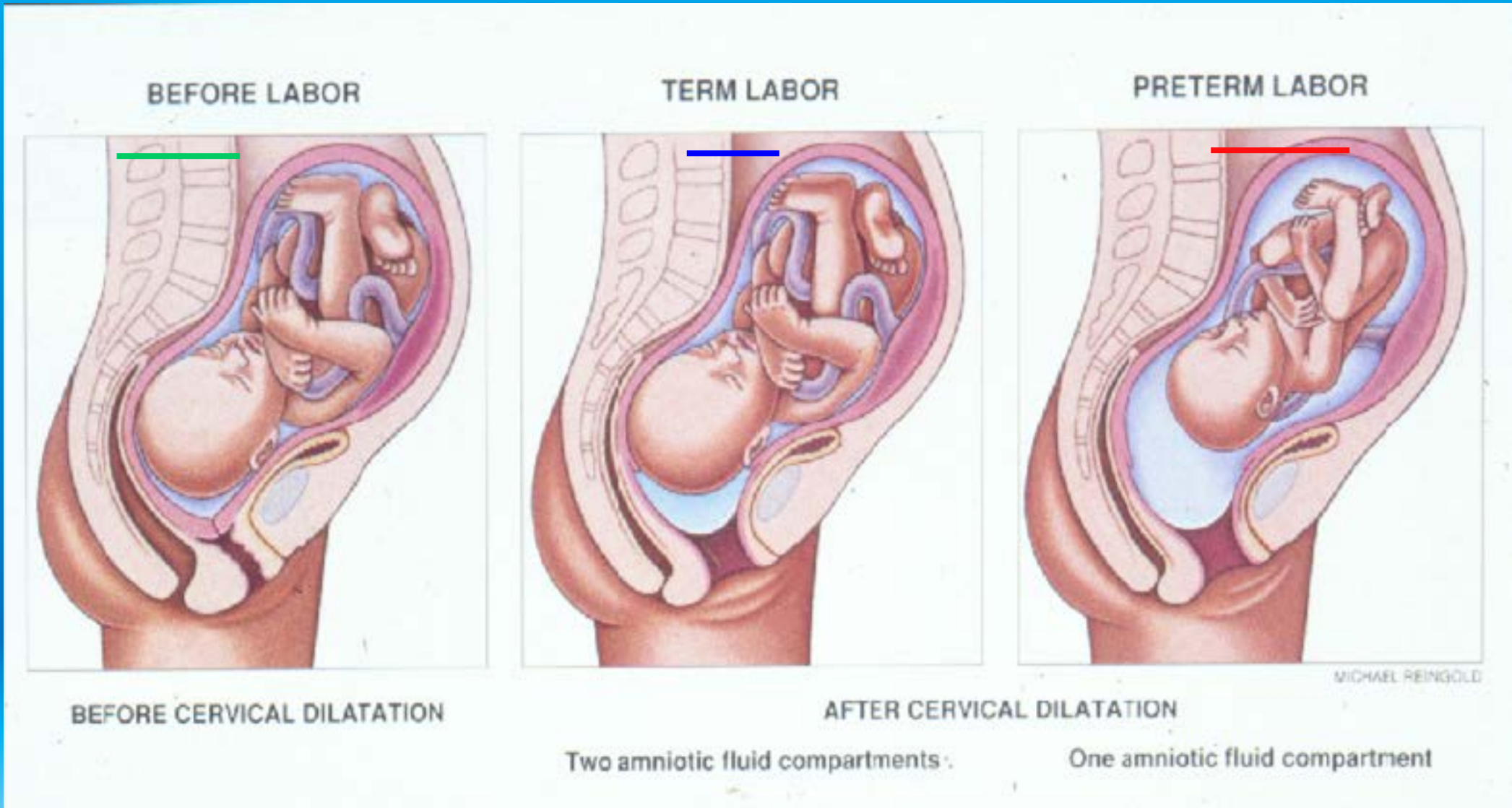
1.	India
2.	China
3.	Nigeria
4.	Pakistan
5.	Indonesia
6.	United States of America
7.	Bangladesh
8.	Philippines
9.	Dem. Rep. of Congo
10.	Brazil



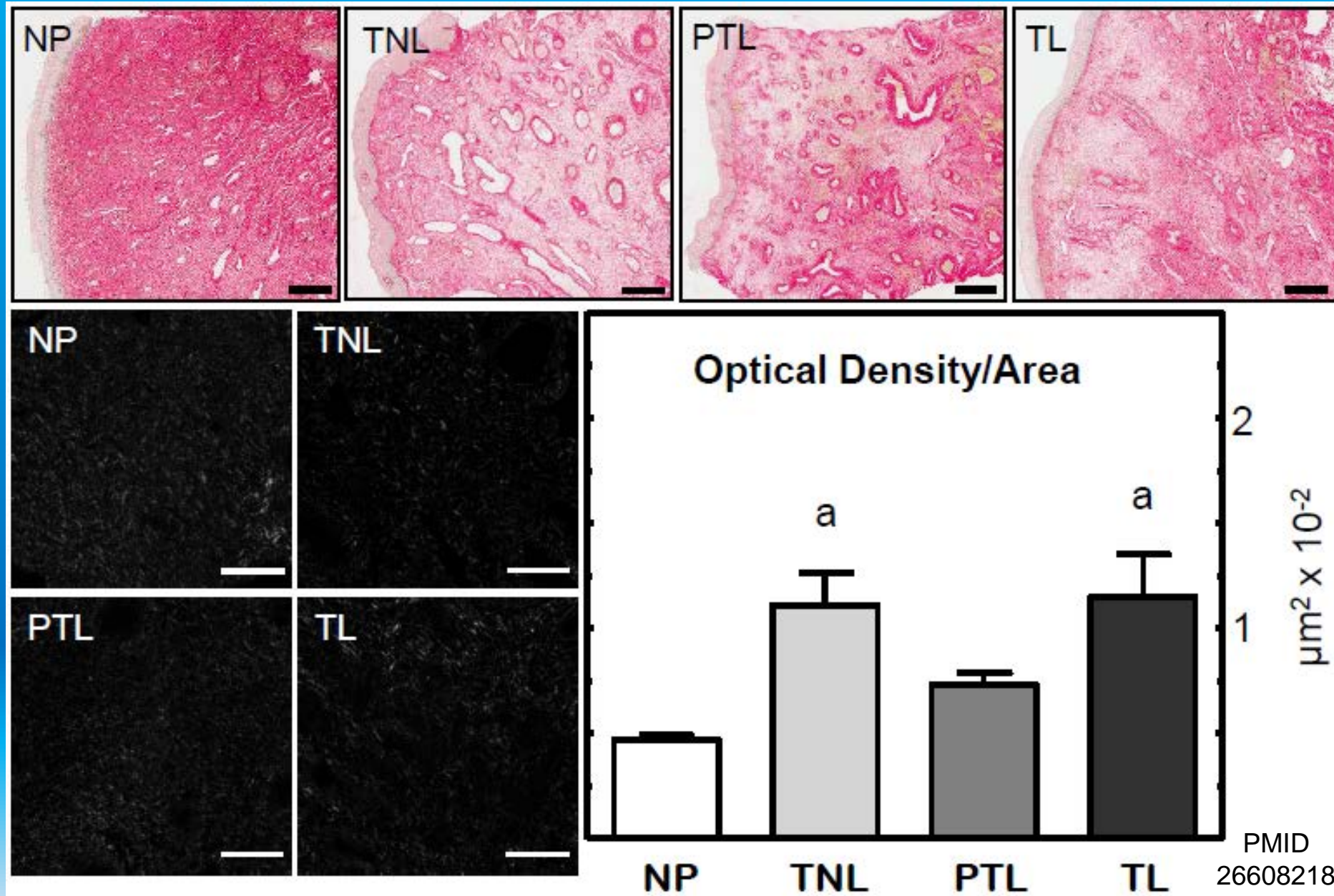
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lysis and implications.

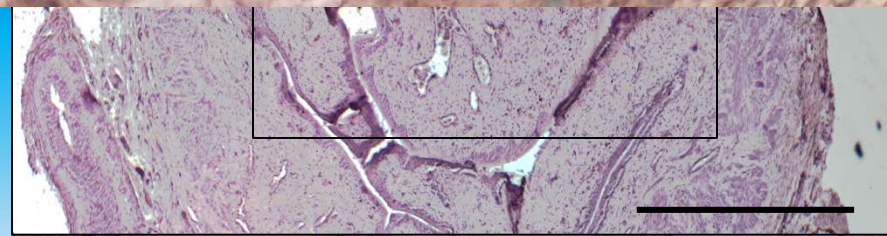
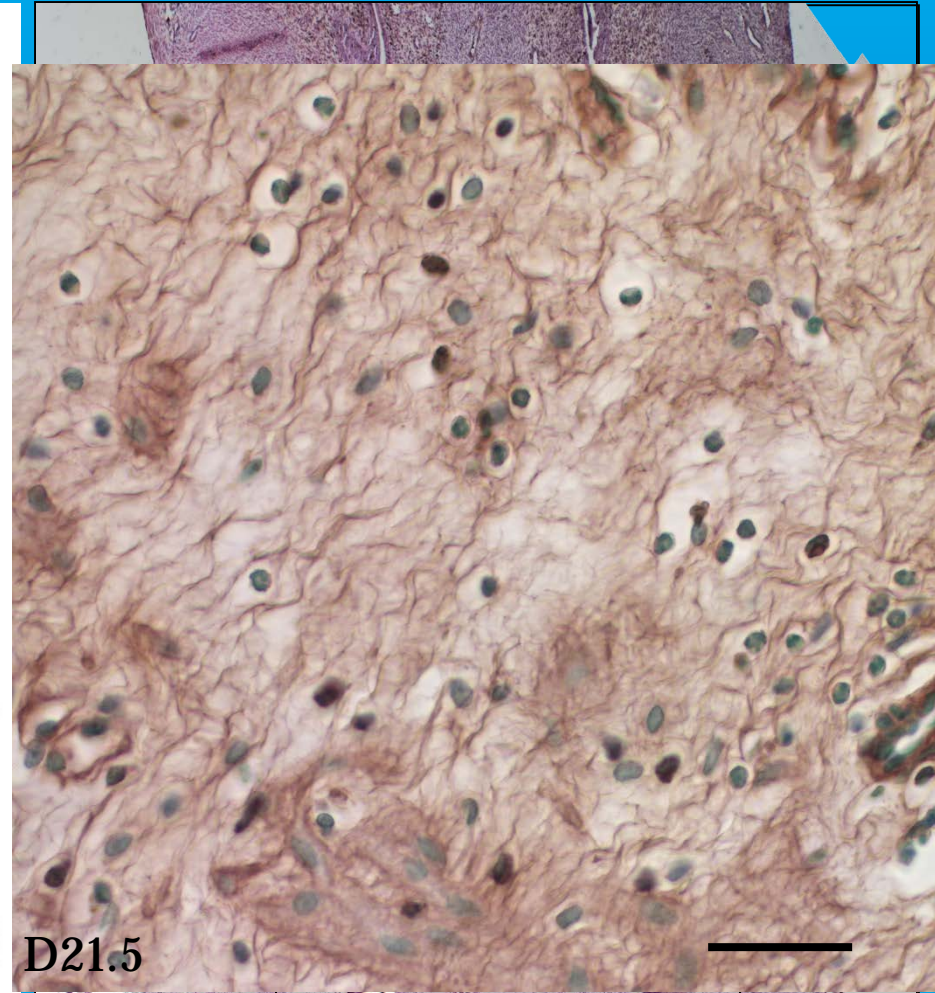
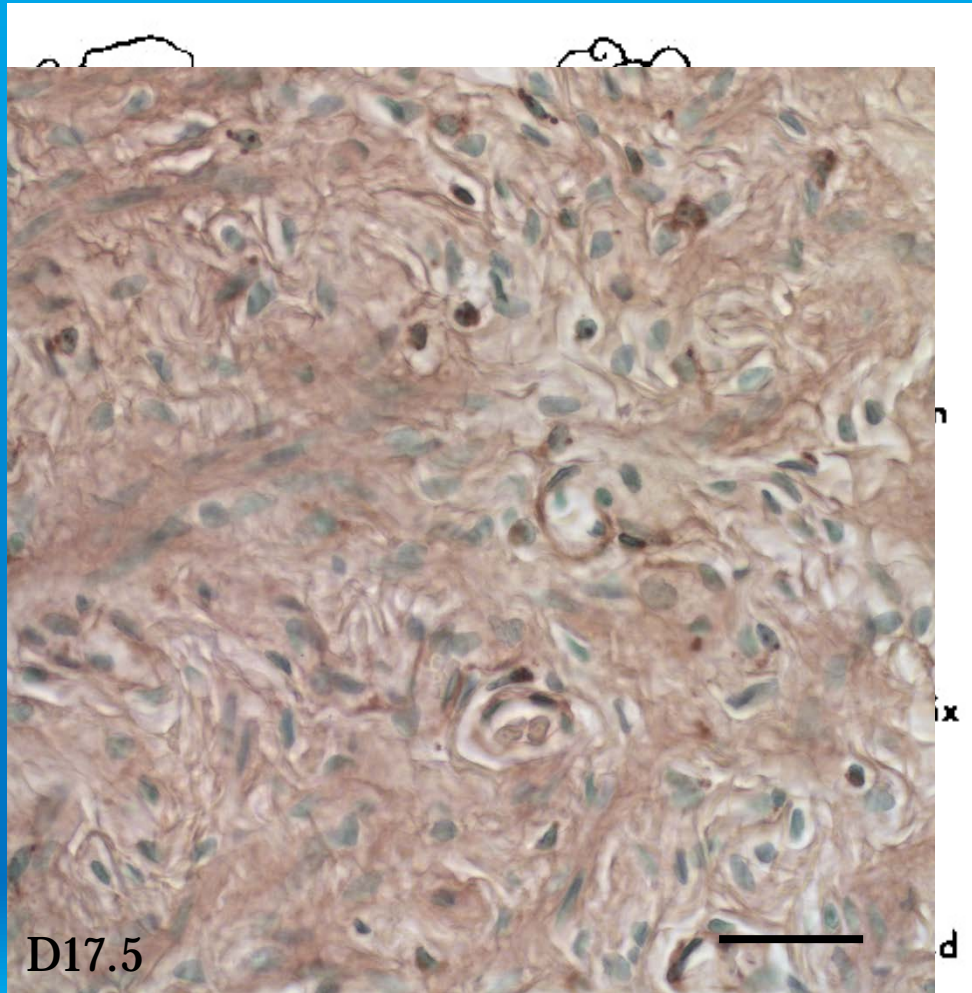
Closed then open case for timing of birth?



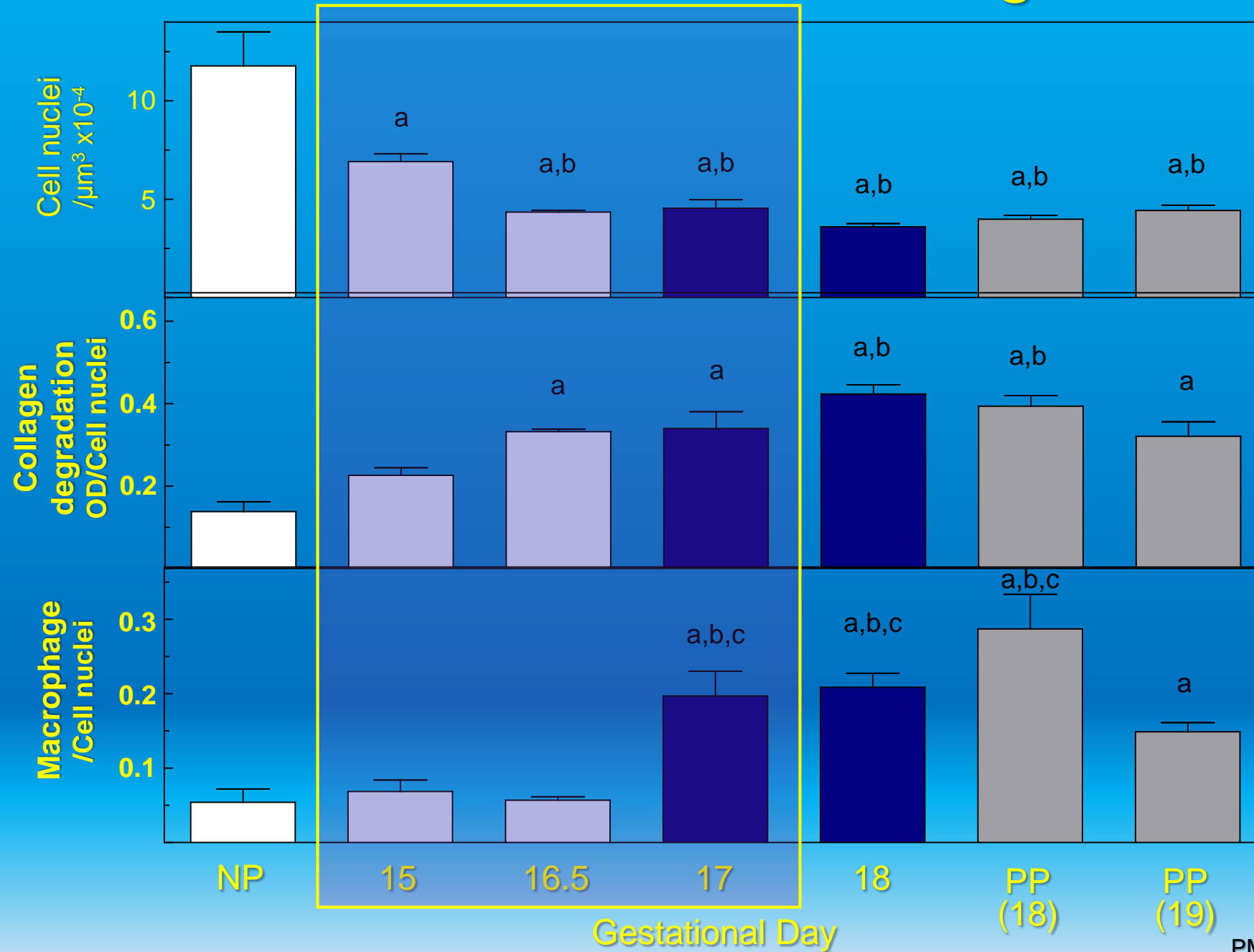
Picrosirius red-stained collagen and optical density analysis of cervix biopsies from nonpregnant (NP), pregnant and immediately postpartum women



Rodent female reproductive tract

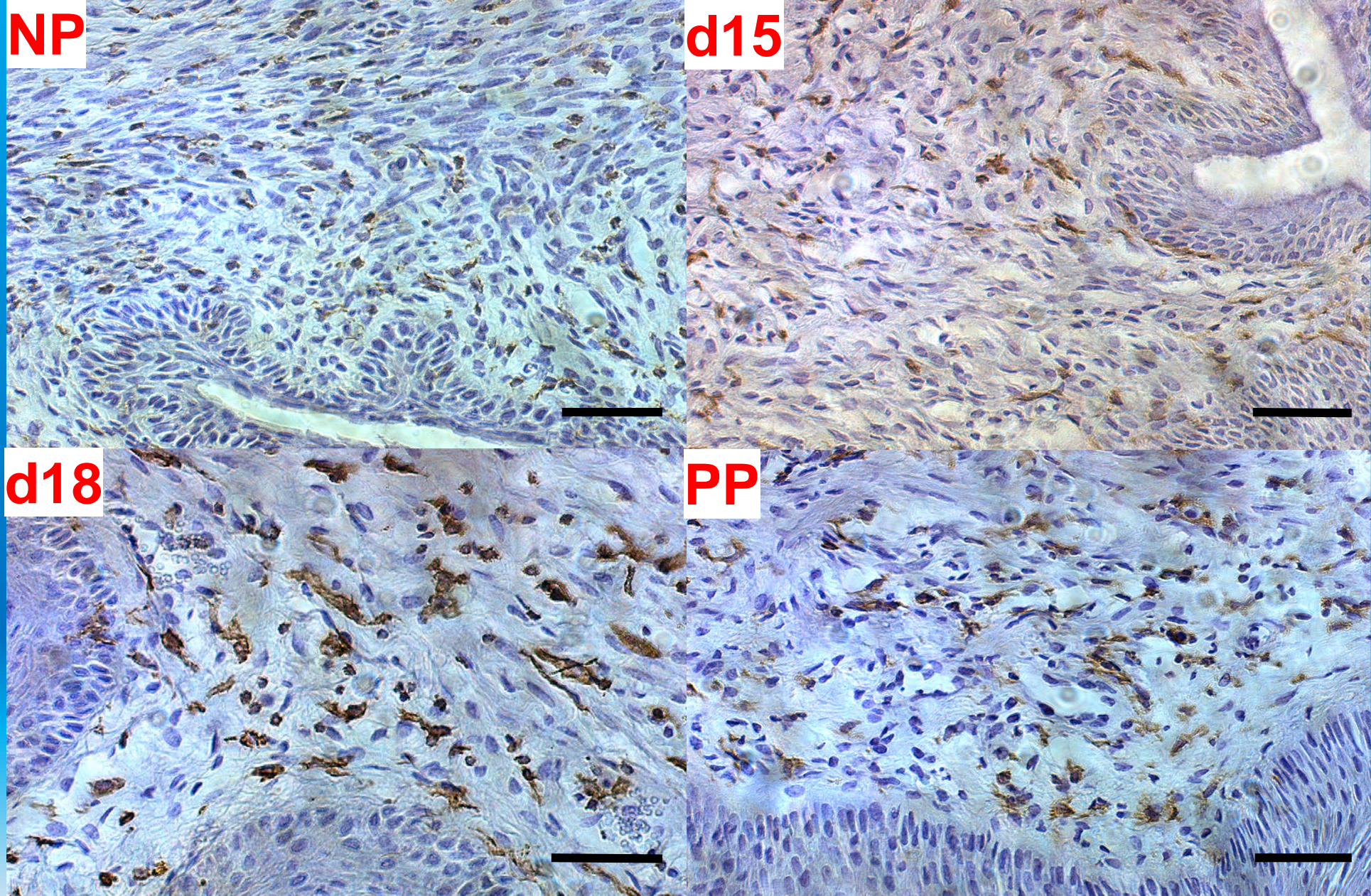


Characteristics of cervix remodeling in mice

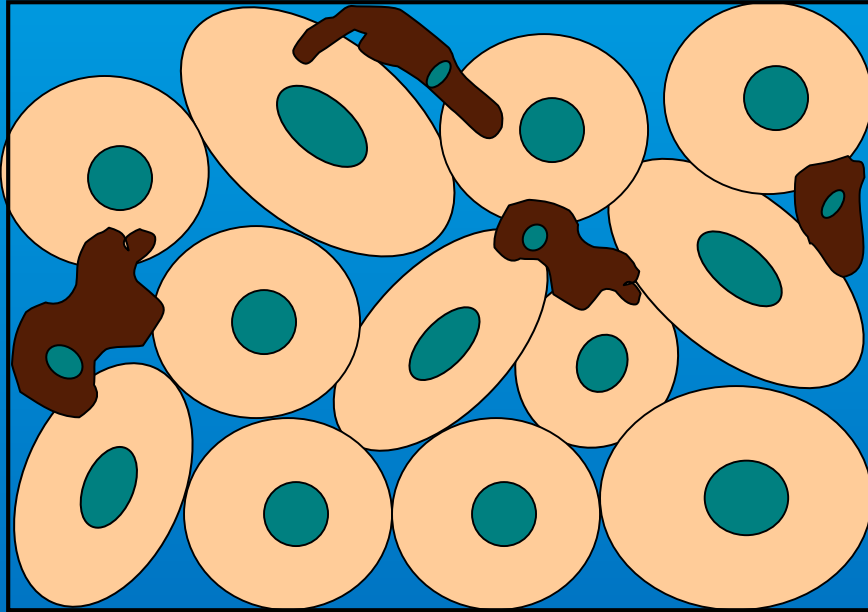




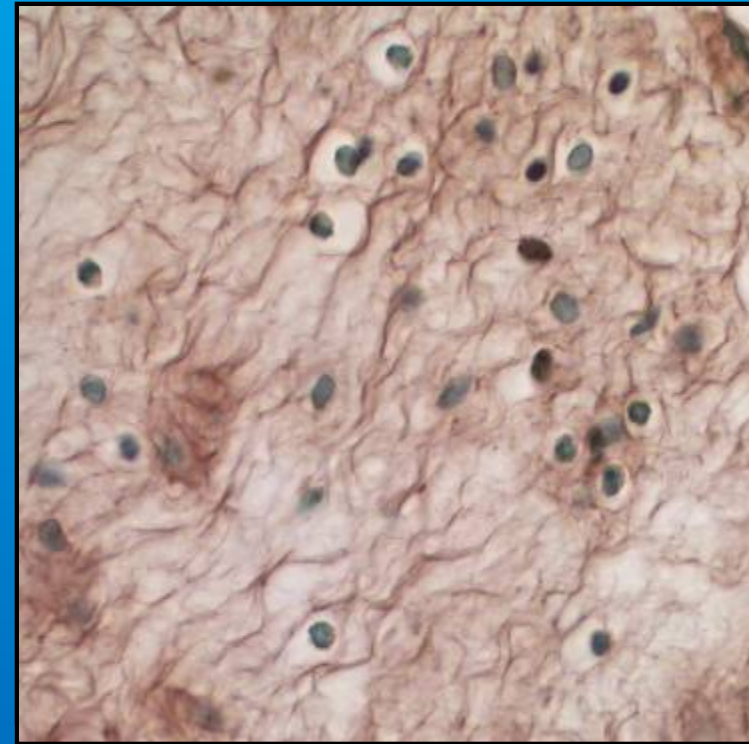
Mφ increase in the murine prepartum cervix



Cervix stroma hypertrophy with pregnancy

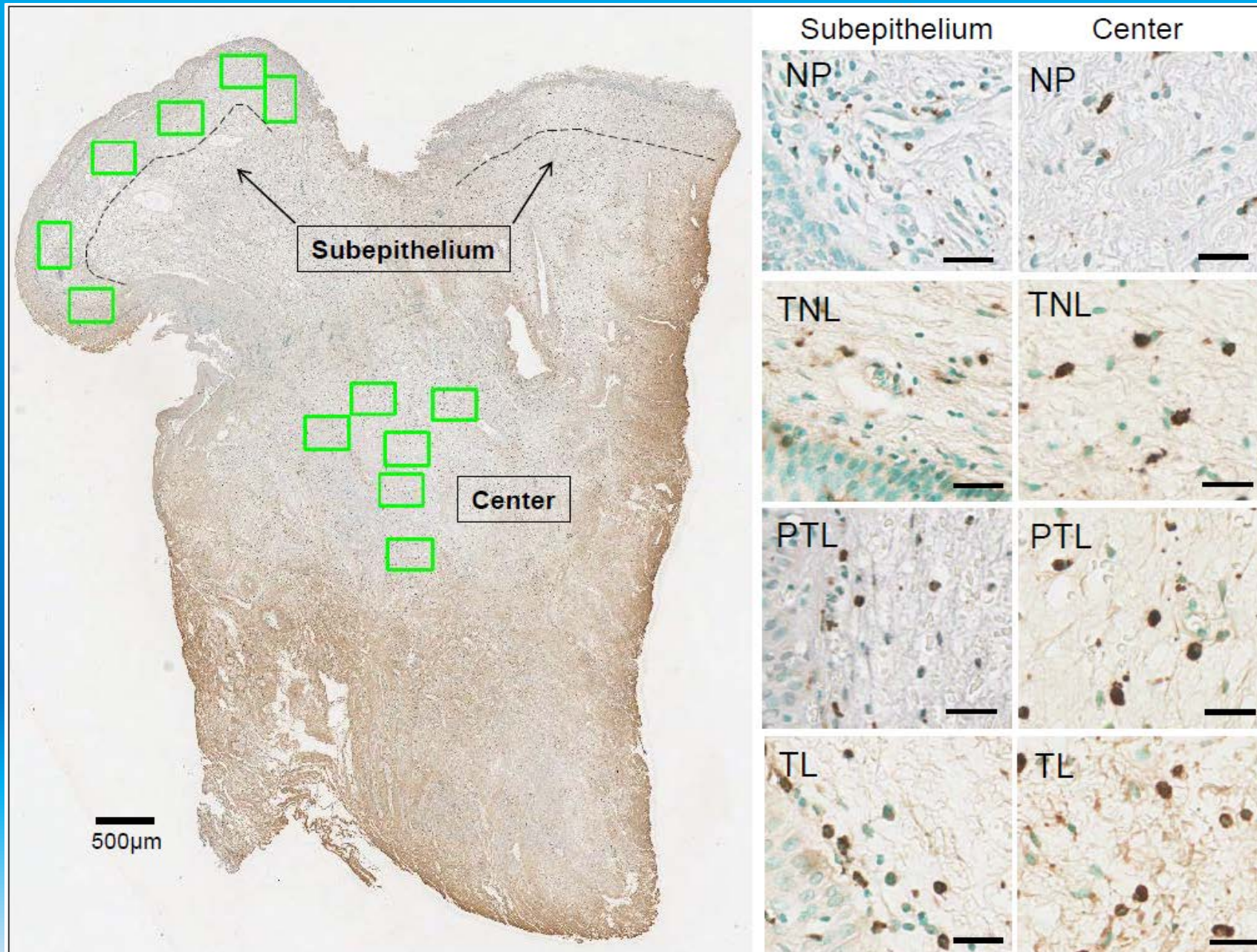


Late Mid-Pregnancy

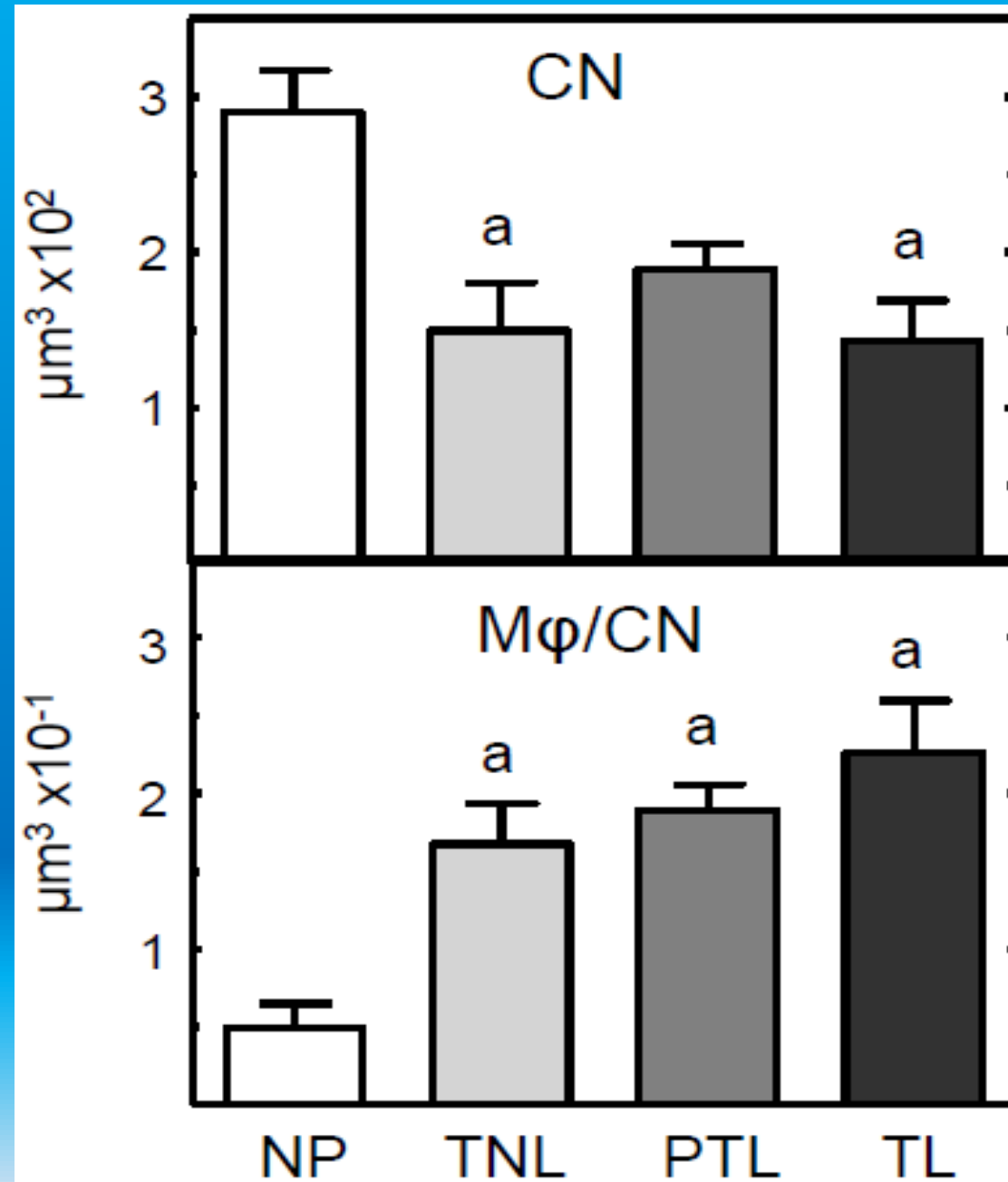


Day of birth

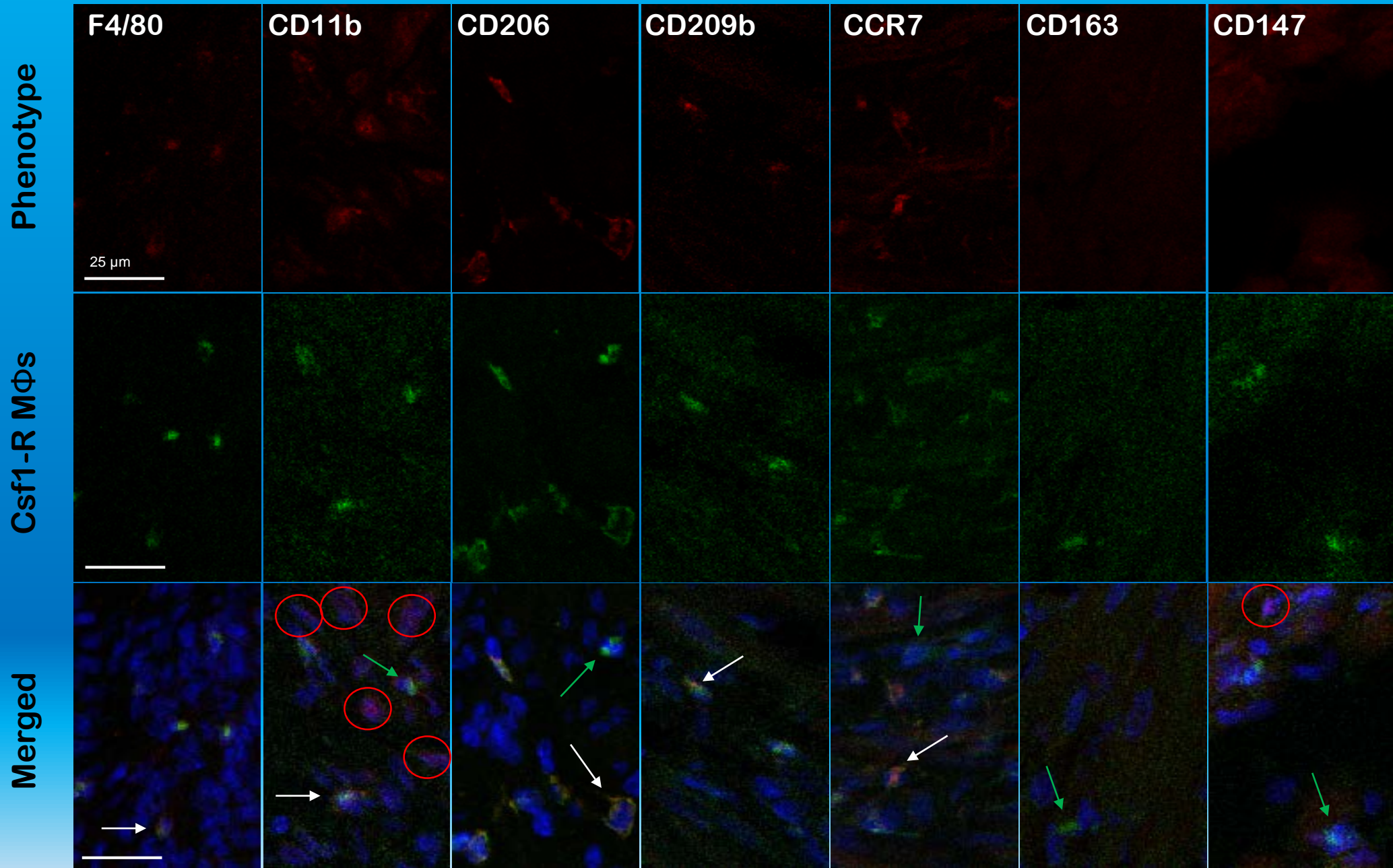
Translational analyses of cervix biospies in women



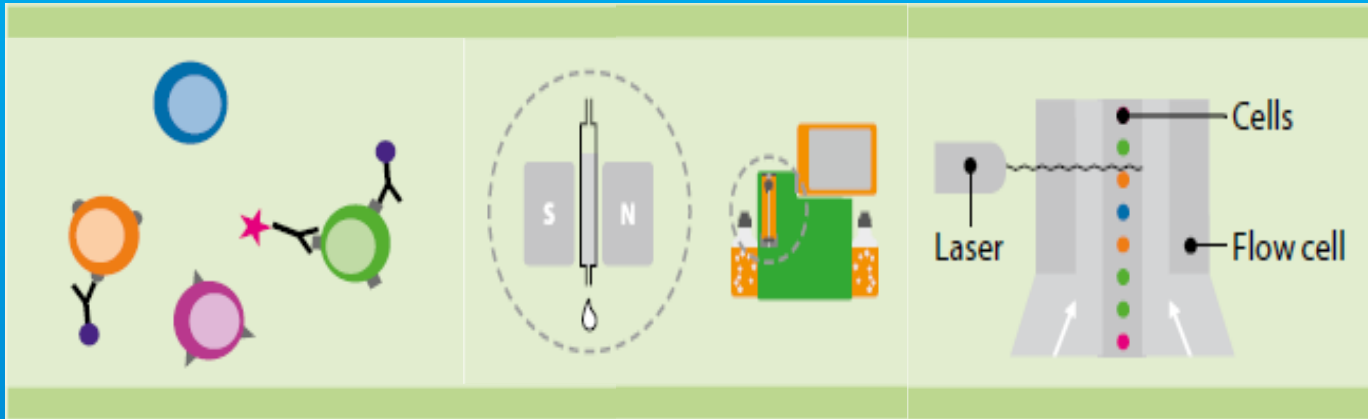
Hypertrophy and increase in resident Mφs in prepartum human cervix



Confocal images of activation markers in M ϕ phenotypes

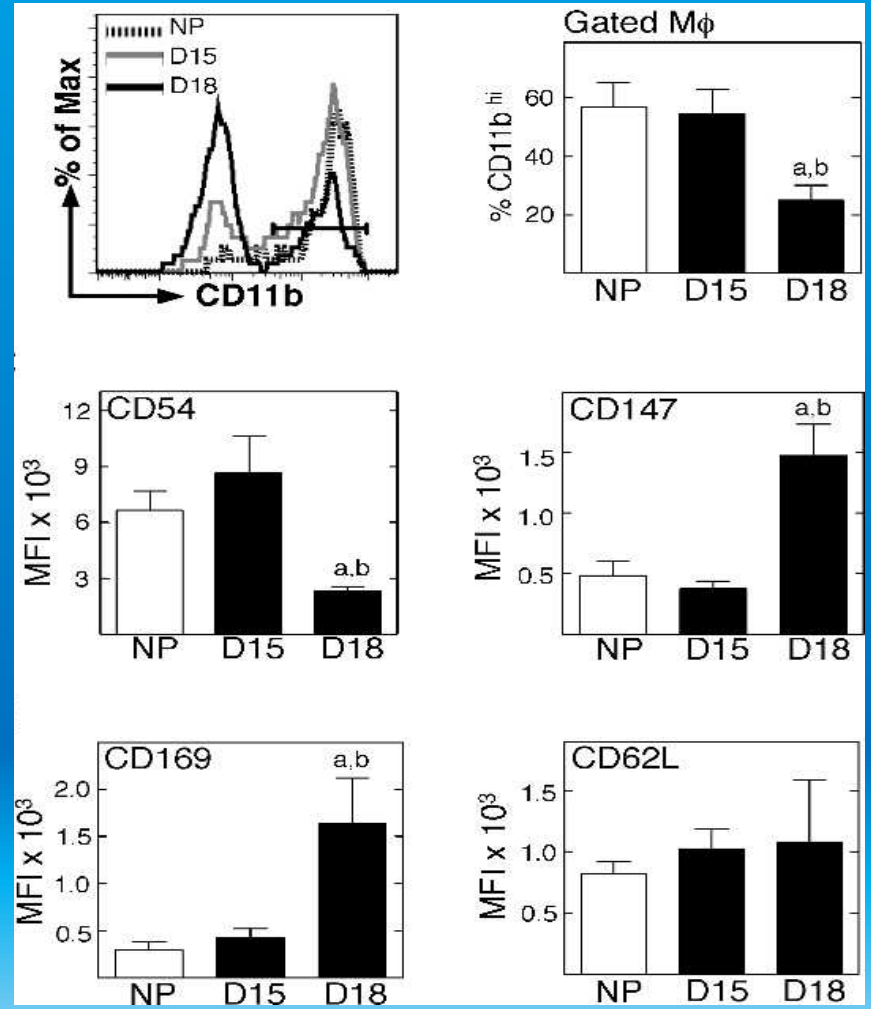
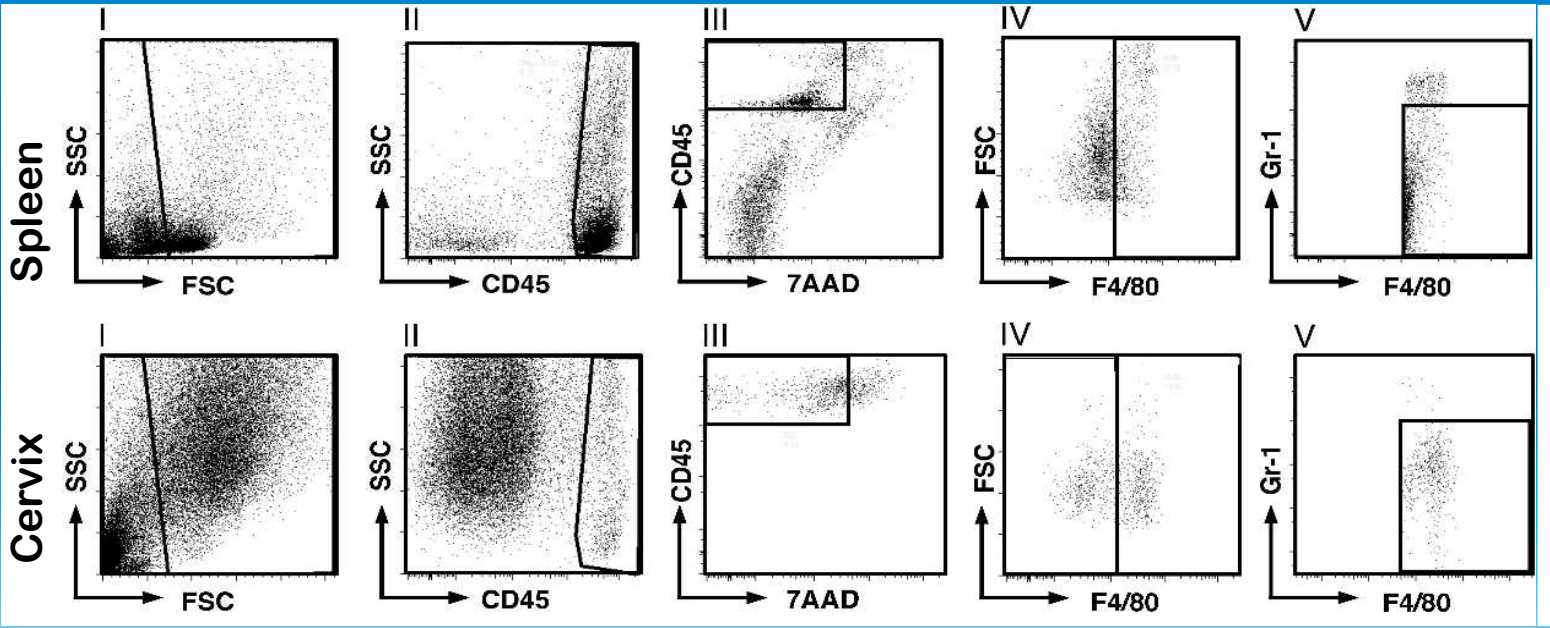


Association of Macrophage Phenotypes in Cervix Remodeling

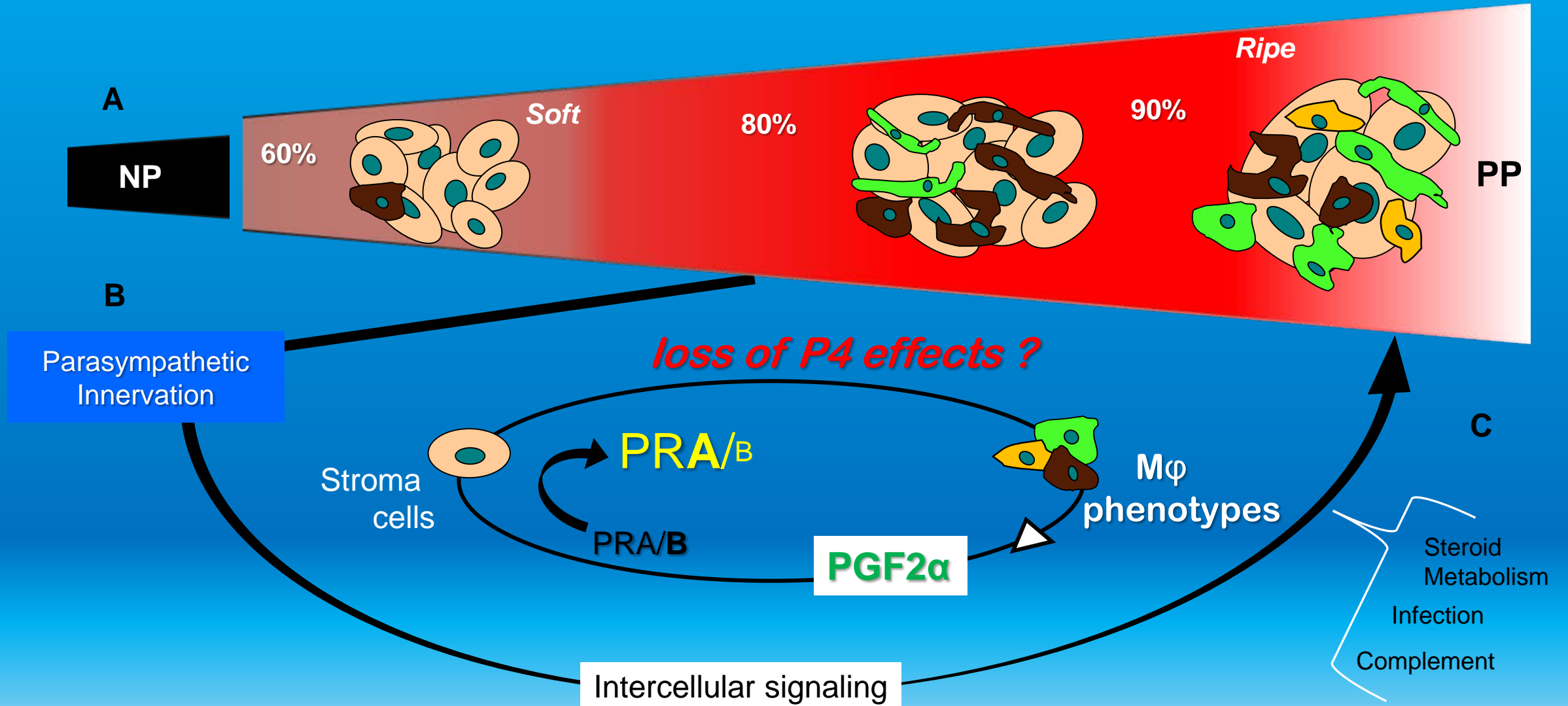


Flow cytometry gating strategy to identify leukocyte populations

Kimberly Payne Ph.D., Associate Professor of Human Anatomy, CHDMM



Final common pathway for cervix remodeling at term and with preterm birth

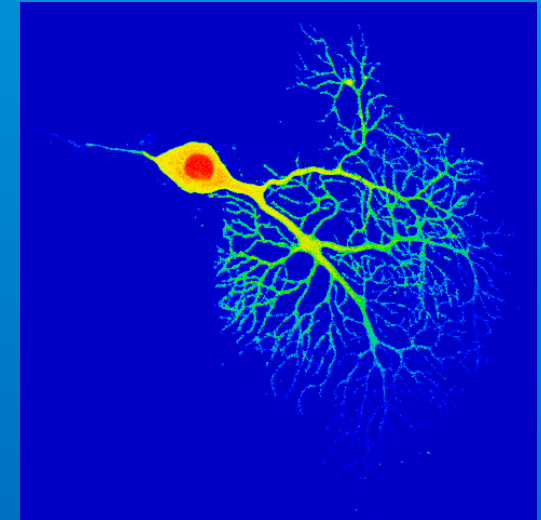




LOMA LINDA UNIVERSITY
SCHOOL OF MEDICINE
ADVANCED IMAGING & MICROSCOPY



Steven M. Yellon Ph.D., Administrative Director
Sean M. Wilson Ph.D., Technical Director
Monica Romero, Core Facility Manager



Medical Research Wing Room A522, x15807

<http://medicine.llu.edu/research/core-facilities/advanced-imaging-and-microscopy-core>



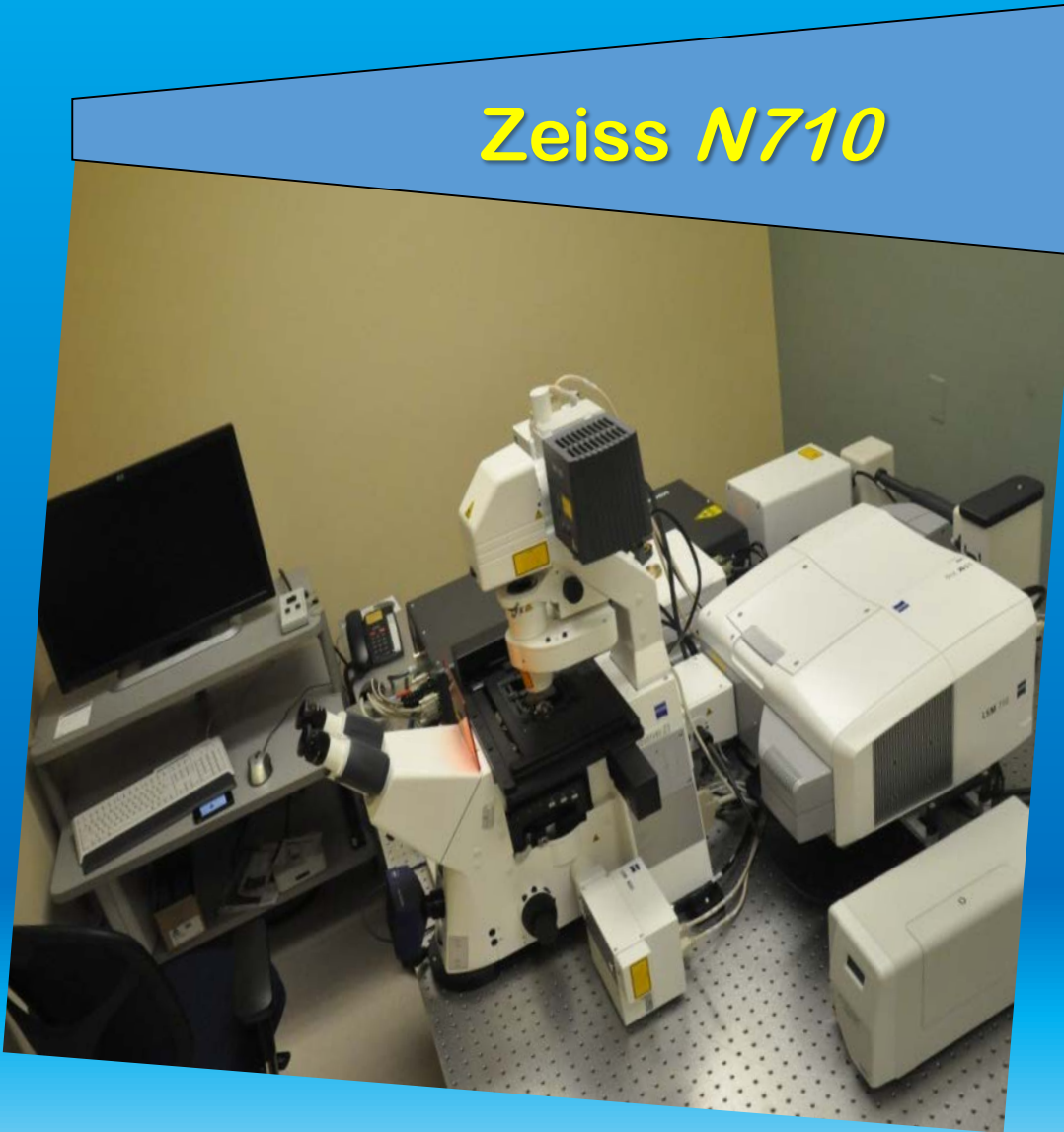
Drs. Steven Yellon, Sean Wilson, and Lawrence D. Longo at the opening of the Advanced Imaging & Microscopy Facility.

LLUSM AIM Vision

To serve the Mission of Loma Linda University, the core facility will meet the educational, training, and research needs of students and investigators with advanced systems to capture and analyze microscopic images.

Laser Scanning Confocal Microscopes

Zeiss N710

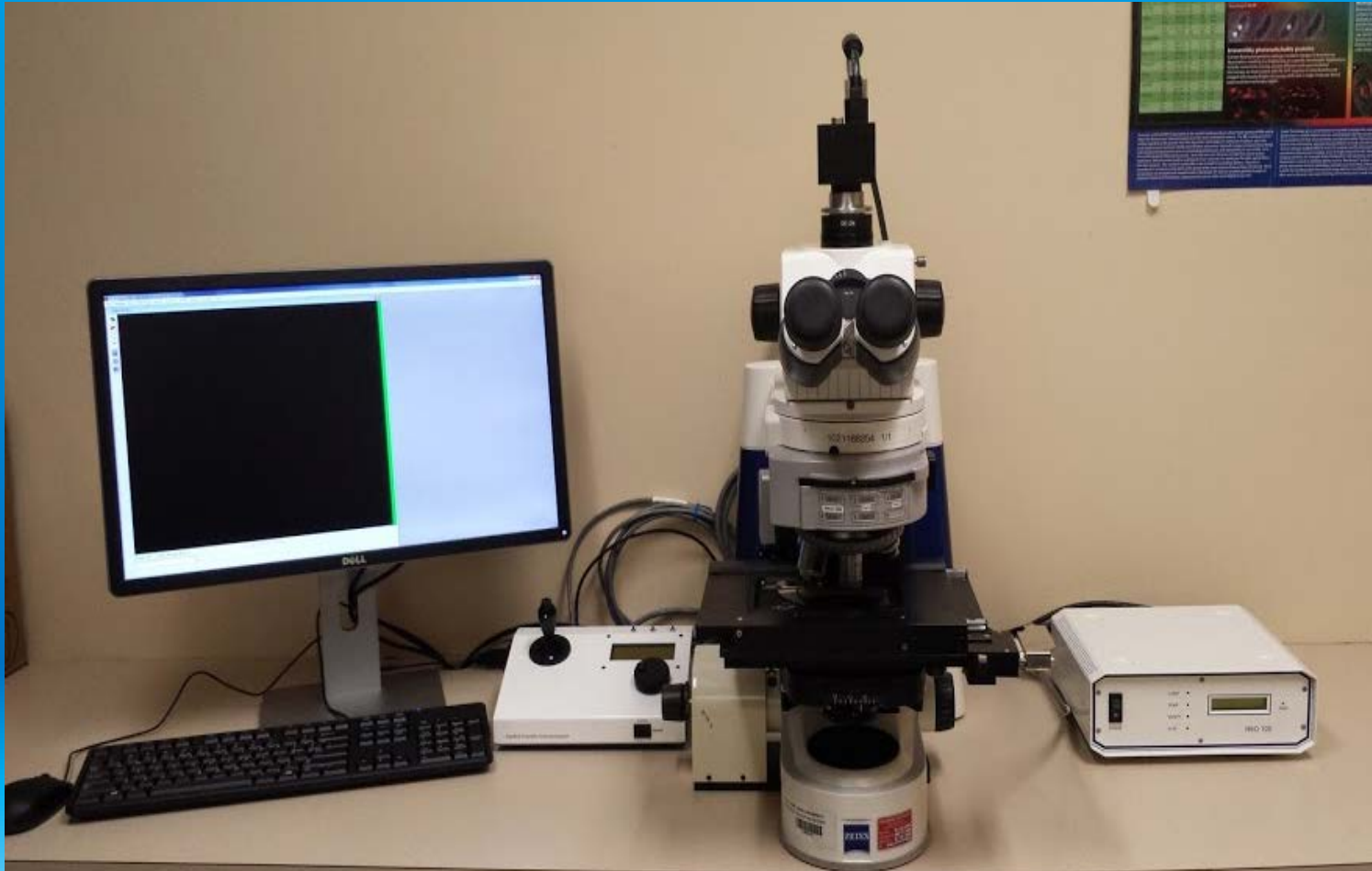


Olympus FV1000

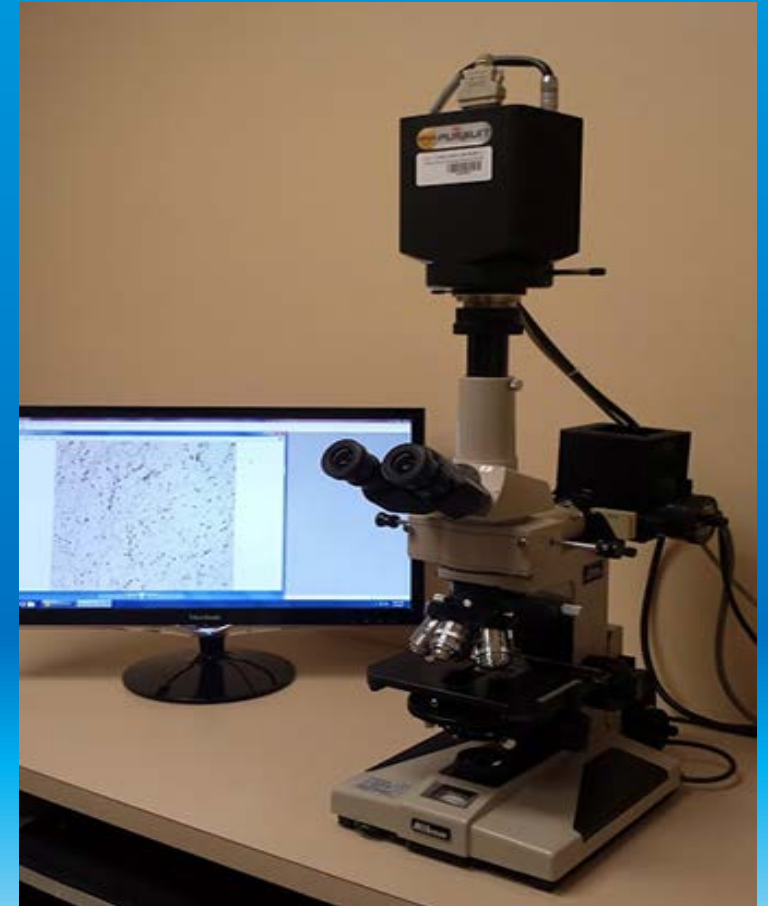


Brightfield and epifluorescence microscopes

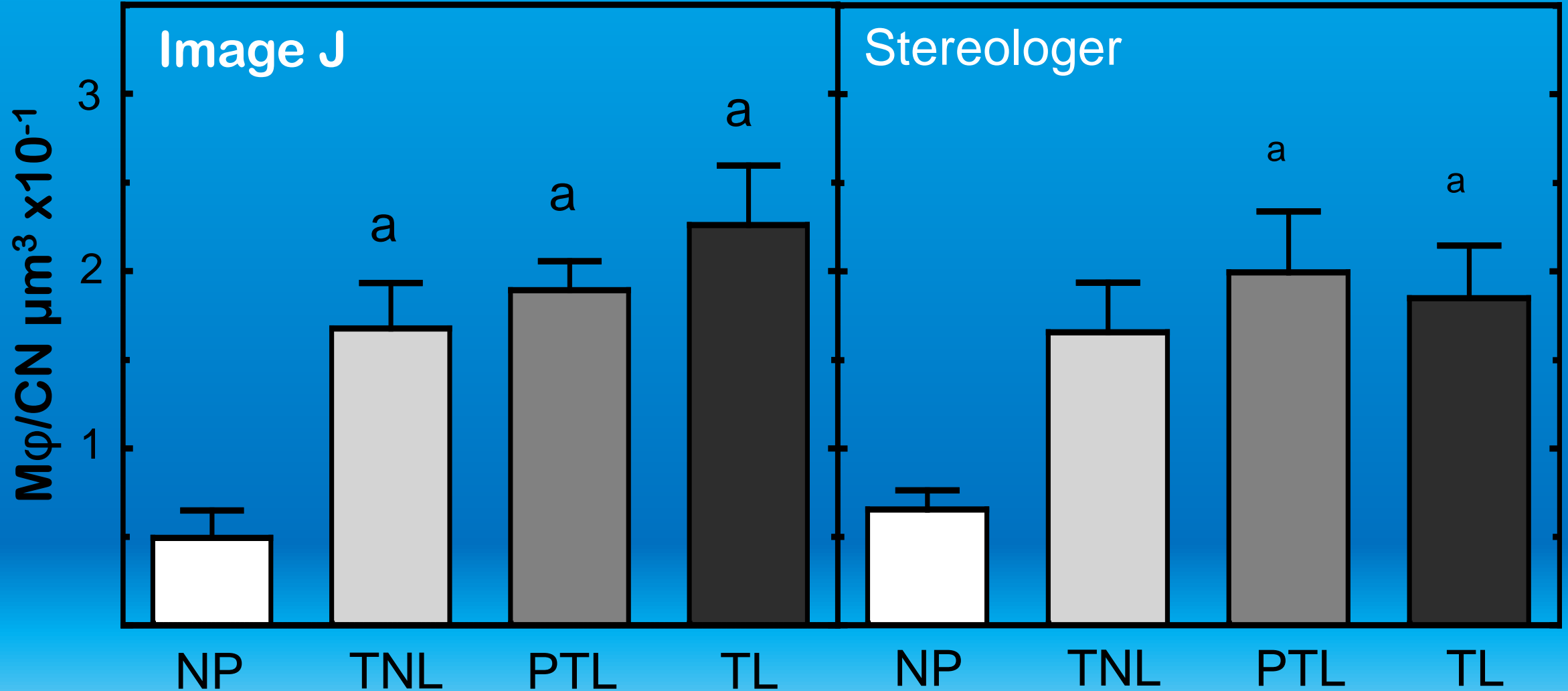
Zeiss Axio Imager A1



Nikon Optiphot



Macrophage density in cervix biopsies from nonpregnant and prepartum women at term and with preterm birth- use of Stereologer



Zeiss stereomicroscope and halogen light source



The core facility has a Zeiss stereomicroscope and halogen light source for tissue and imaging chamber preparation.

Work stations and Image analyses systems



- ❖ **Stereologer**
unbiased image analysis

- ❖ **Imaris**
tracking and analysis of cells and organelles, tracking of cell division, lineage analysis, rotational and translational drift correction, angle measurements, a wide range of plugins (XTensions) and advanced interactive plotting
<http://www.bitplane.com/>

Acknowledgments

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Research assistants

Anne Heuerman
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Jessica Steinbach

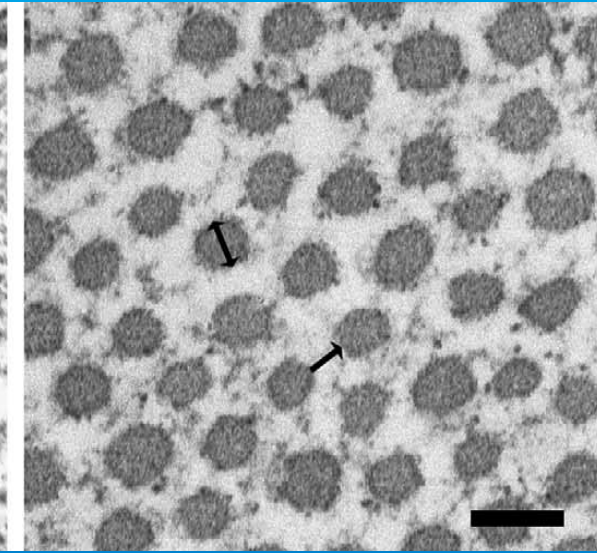
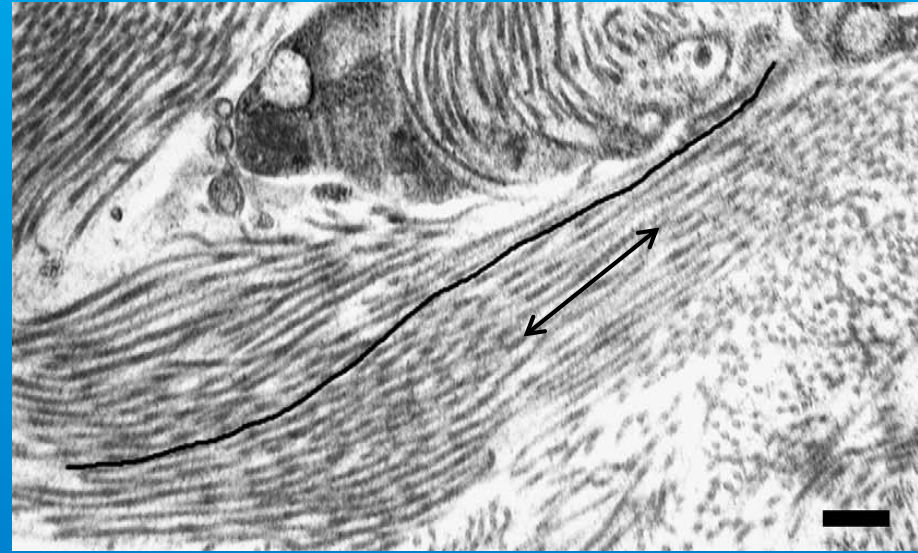
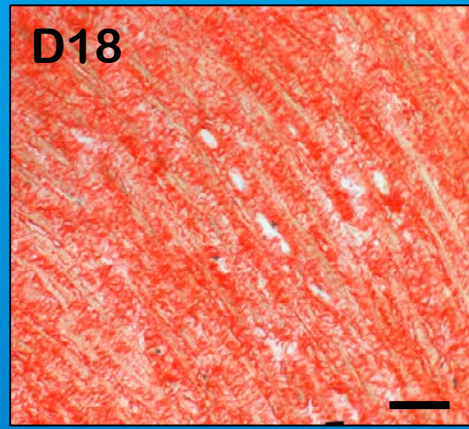
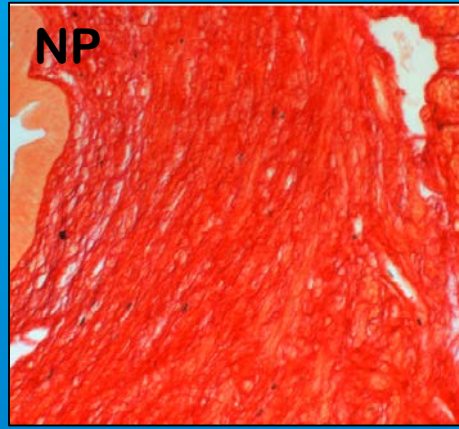
Co-investigator

Michael A. Kirby, Ph.D.



Assessment extracellular collagen structure and content in cervix by TEM and birefringence of picosirius red stain

Mouse



Women

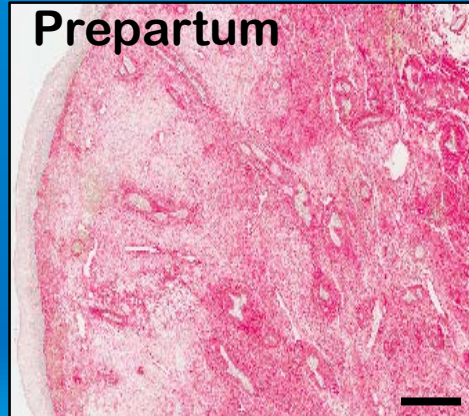
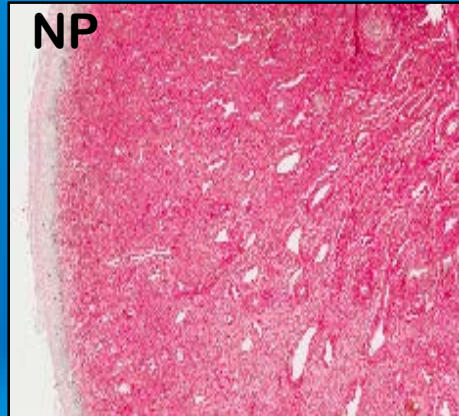


Table II Mean fibril diameter, interfibrillary distance, and length (in nm) at term (day 21) after treatment with PGE2 (rat)

	<u>Diameter</u> (nm) (mean ± SEM)	<u>Central interfibrillary distance</u> (nm) (mean ± SEM)	<u>Peripheral interfibrillary distance</u> (nm) (mean ± SEM)	Length (nm) (mean ± SEM)
PGE2	58 ± 3	30 ± 2	34 ± 2	2268 ± 177
Control	53 ± 3	20 ± 2	24 ± 3	2141 ± 310
<i>t</i> test	<i>P</i> = .07	<i>P</i> < .001	<i>P</i> = .002	<i>P</i> = .51

Table I Mean concentration of organized collagen at term (day 21) after administration of selective and nonselective PGE2 agonists (rat)

	% Birefringence (mean ± SEM)	Dunnett's test <i>P</i> value
Control	21 ± 2	
PGE2 (nonselective)	14 ± 1	.009

PMIDs 16325747,26608218

PMID15746668