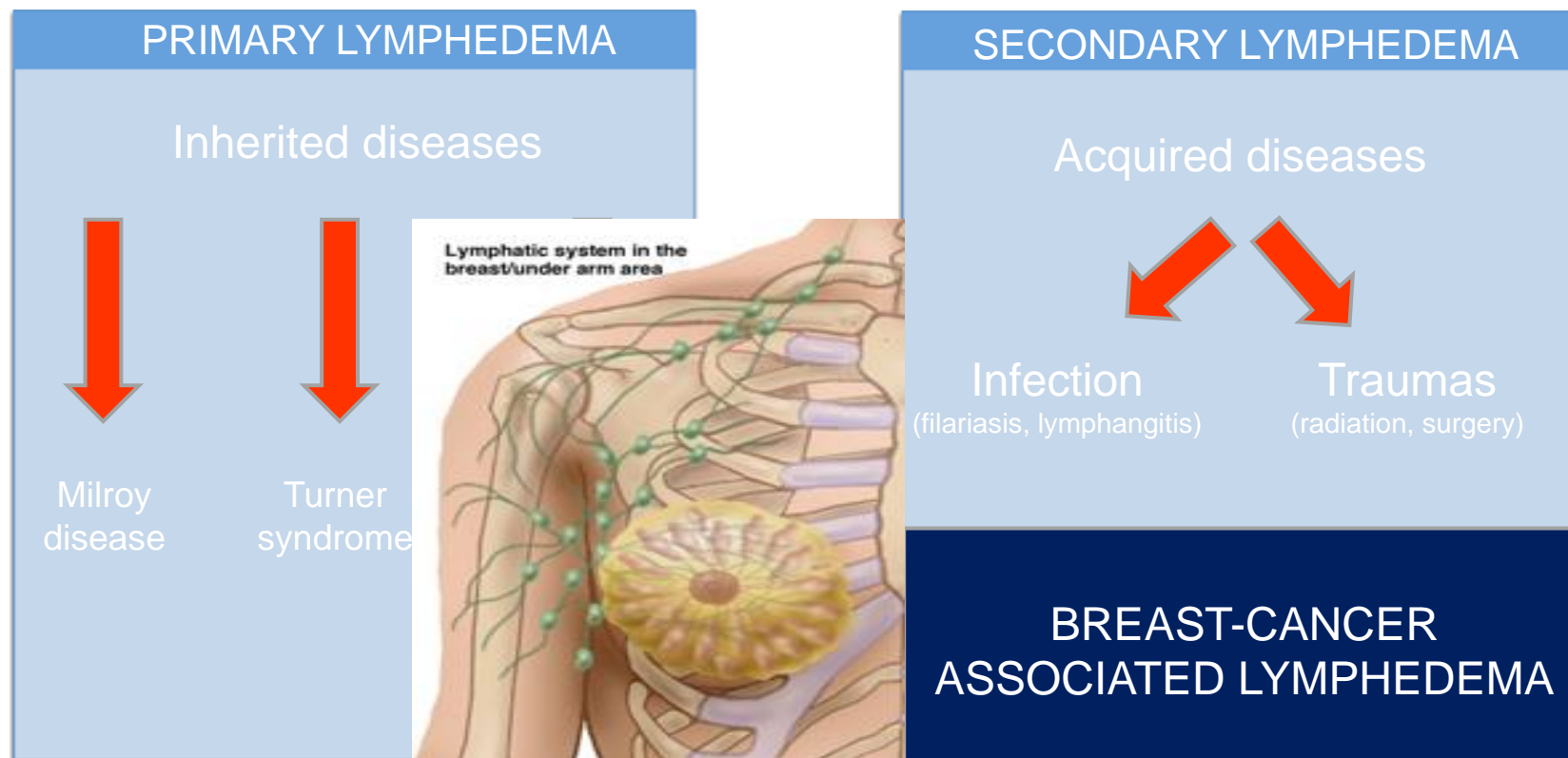


# Lymphatic vasculature requires estrogen receptor alpha signaling to protect from lymphedema

Florent MORFOISSE  
French Angiogenesis Society  
24-04-2017

# Overview of lymphedema

- ❖ Loss of lymphatic function
- ❖ Accumulation of fluids, fat and fibrosis in arm/leg/genitals
- ❖ Lifelong disabling condition without curative treatments



# Gender/Hormone issue in lymphedema

## PRIMARY LYMPHEDEMA

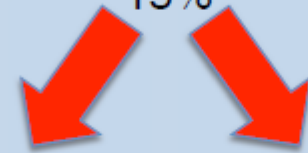


Hormonal implication?

## BREAST CANCER-ASSOCIATED SECONDARY LYMPHEDEMA

Breast Cancer

15%



Hormone  
Therapy

Cancer surgery/  
Chemotherapy/  
radiotherapy/

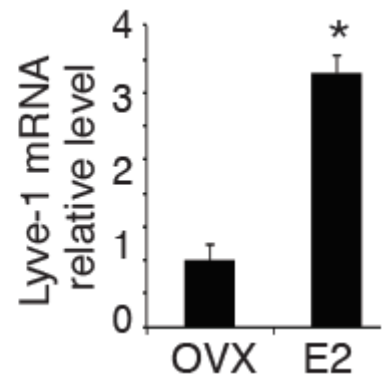
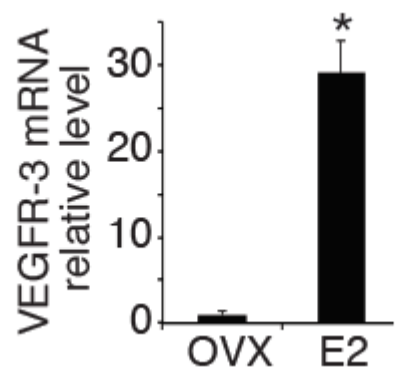
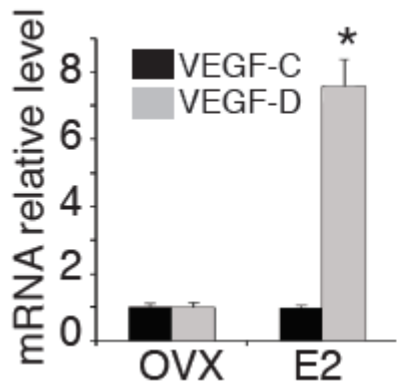
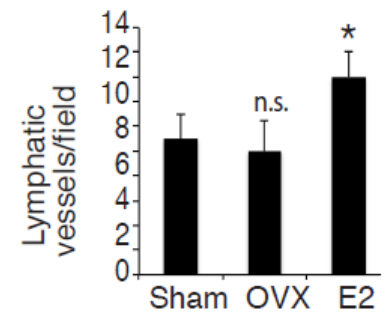
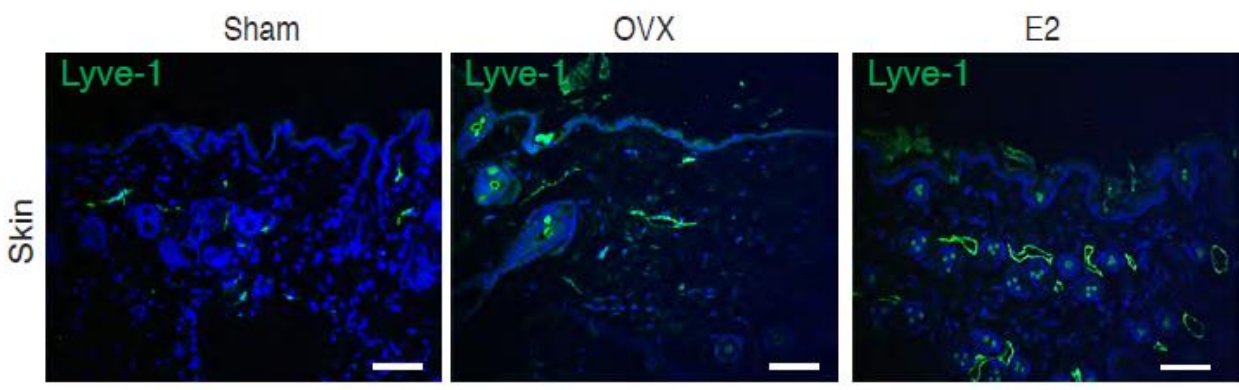
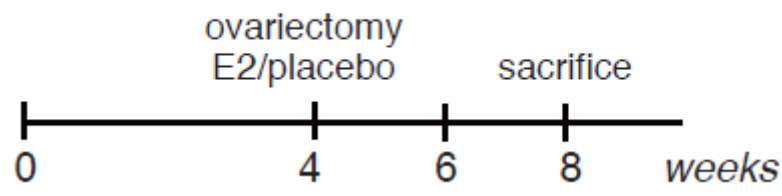


Estrogen  
inhibitors



Ovarian  
Toxins

# Estradiol displays pro-lymphangiogenic properties



# A lack of animal model for BC-associated lymphedema

- ❖ Tail lymphedema model

(Rutkowski, Microvasc Res, 2006)

- ❖ Chy mice (vérif statut VEGFR3)

(Karkkainen et al, PNAS, 2001)

- ❖ Hind limb model

(Oashi et al, Ann Plast Surg, 2012)

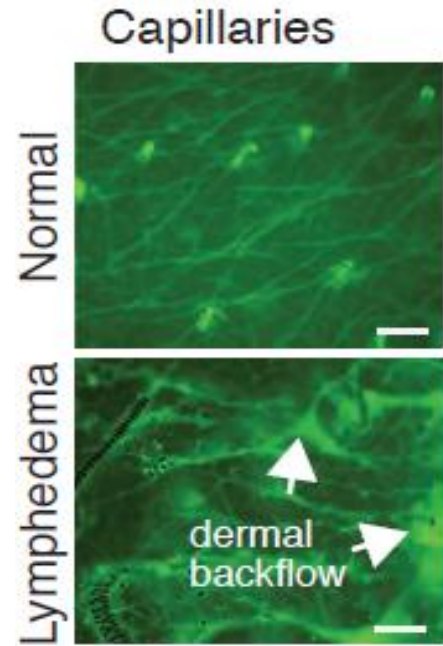
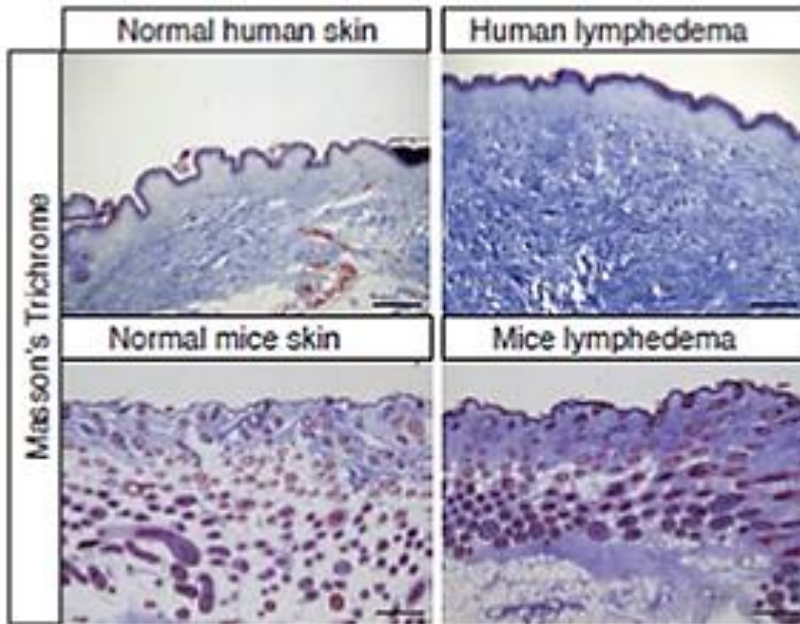
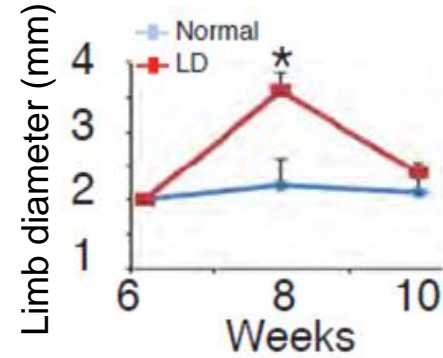
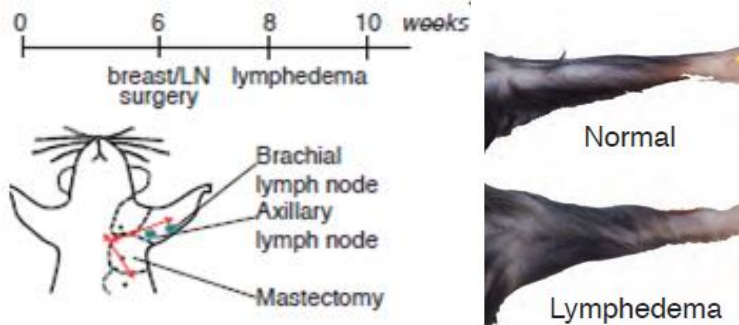
Do not reproduce the human pathology

BREAST CANCER-ASSOCIATED  
SECONDARY LYMPHEDEMA

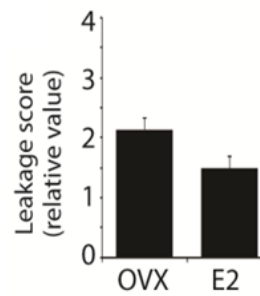
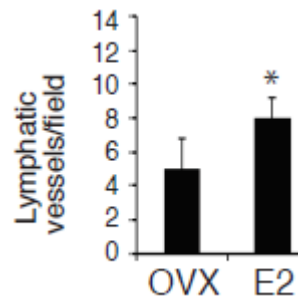
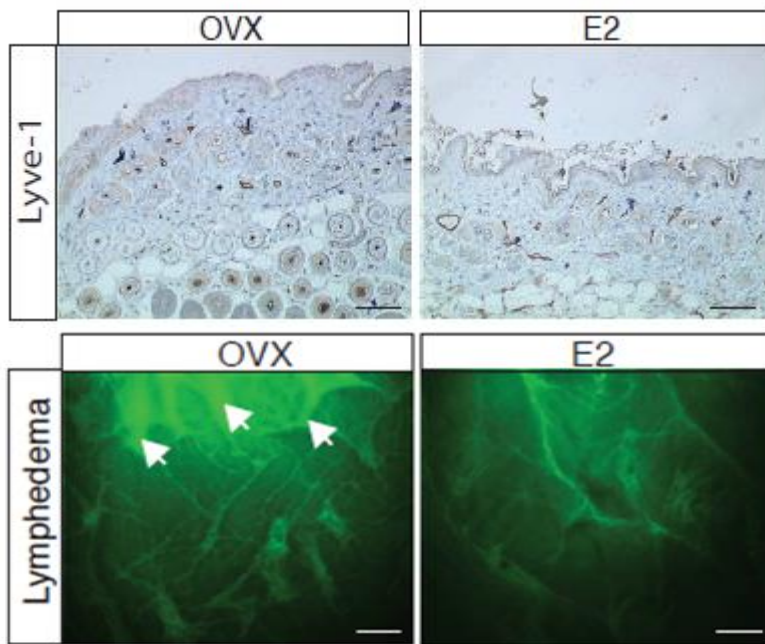
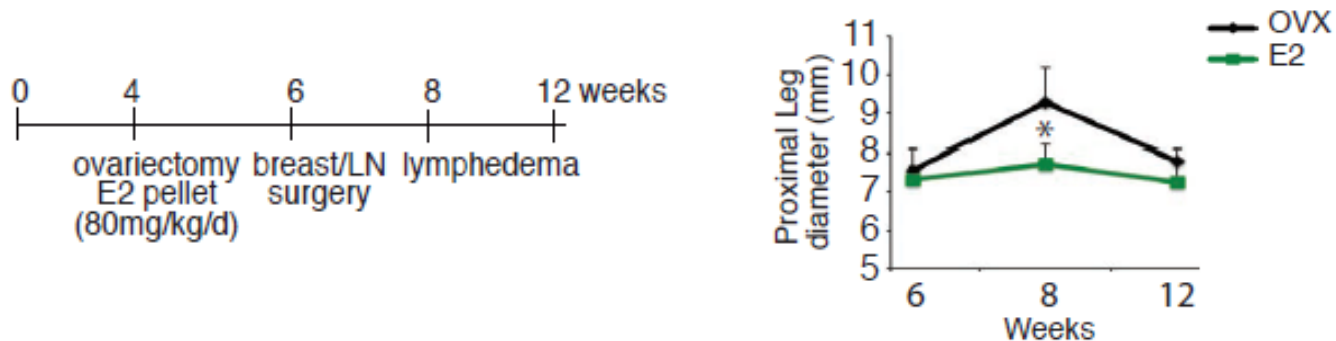


Murine model?

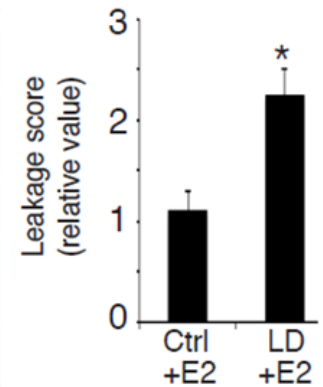
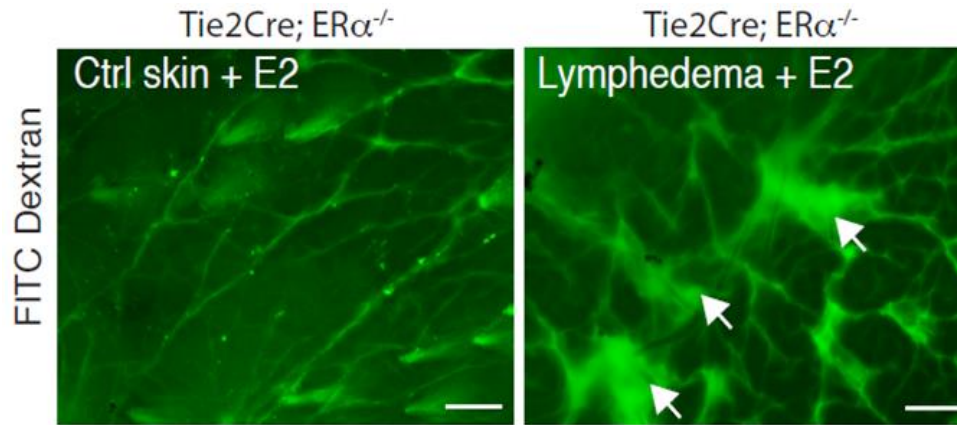
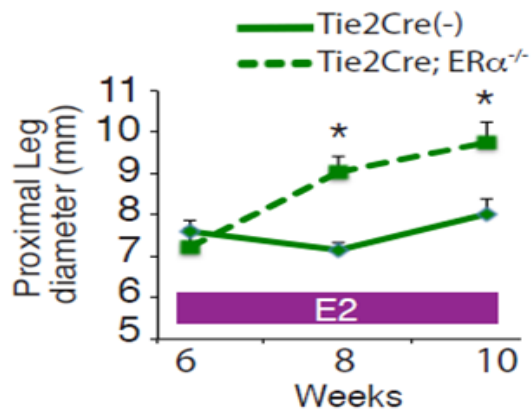
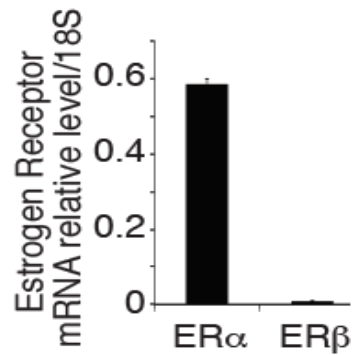
# Murine model related to human BC-associated lymphedema



# Estradiol treatment exhibits protective effects on lymphedema

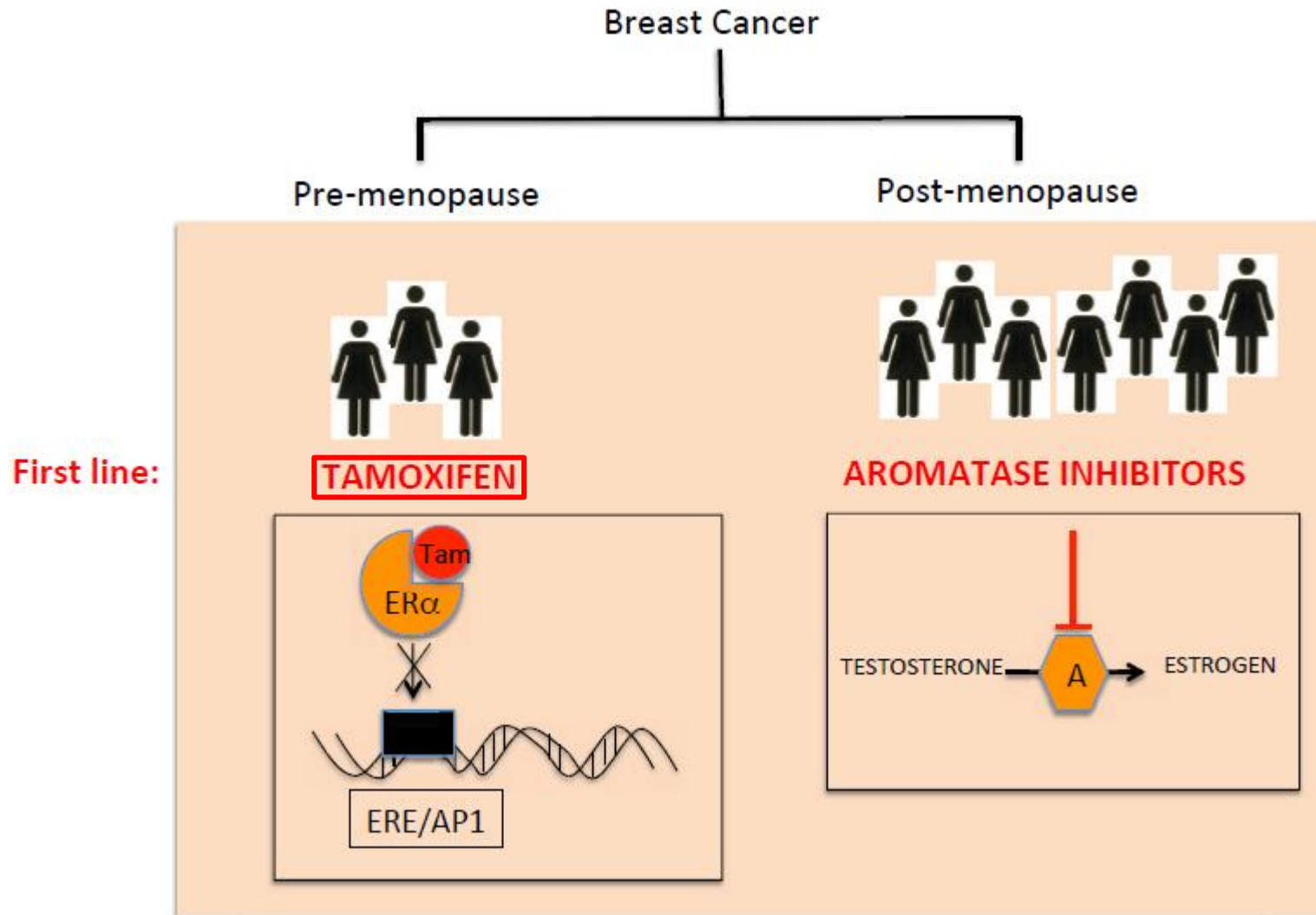


# These effects are mediated through ER alpha

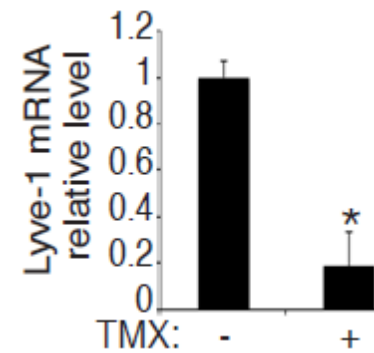
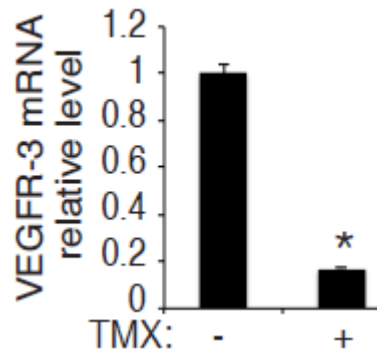
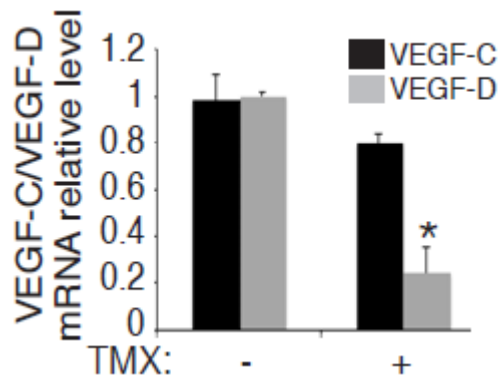
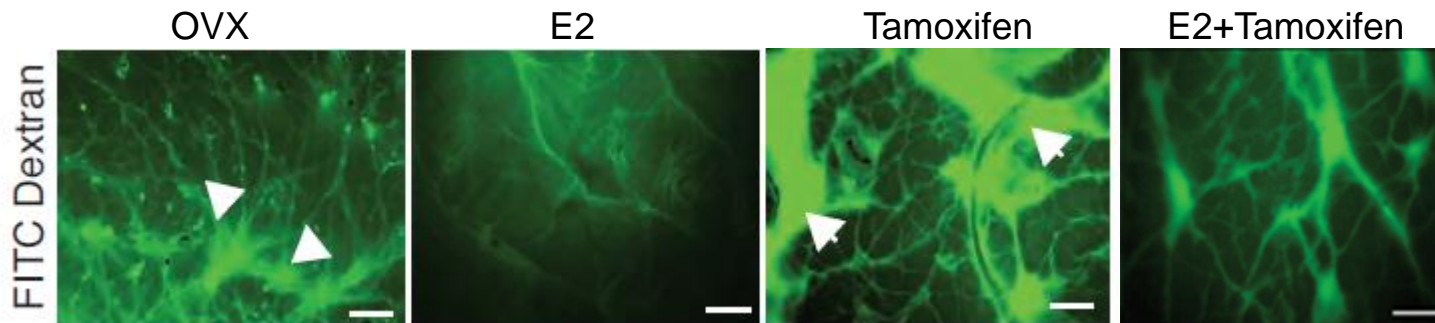
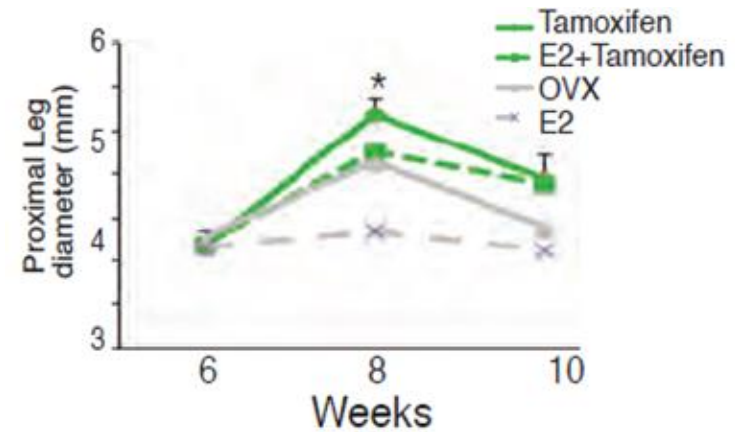
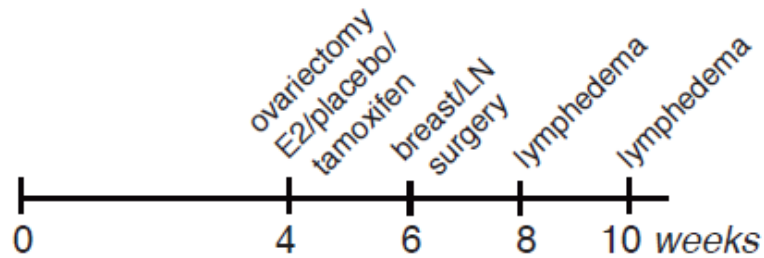




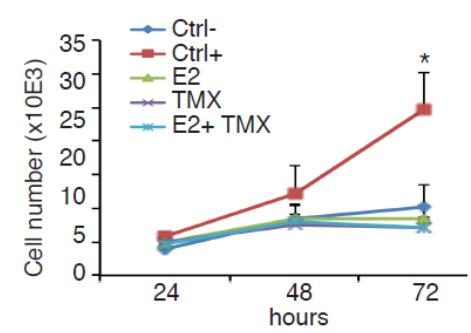
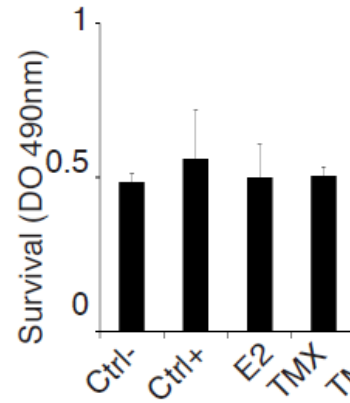
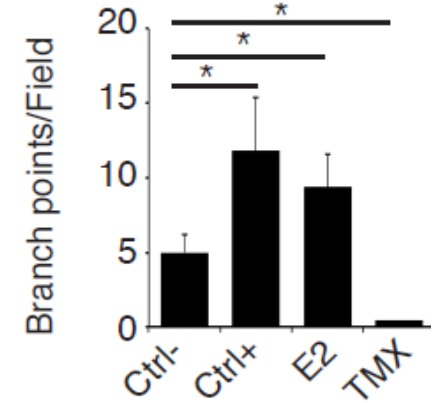
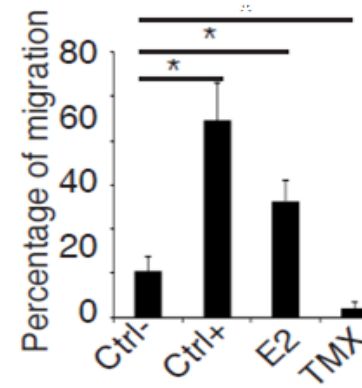
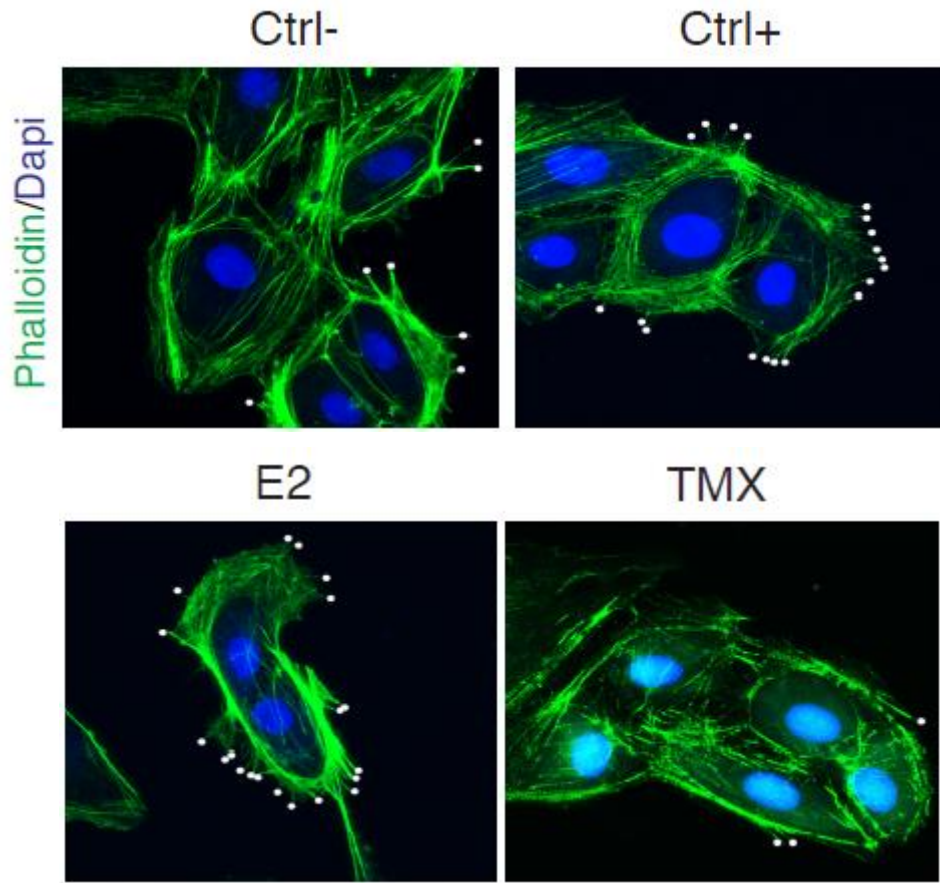
# Hormone therapy for ER-positive breast cancer



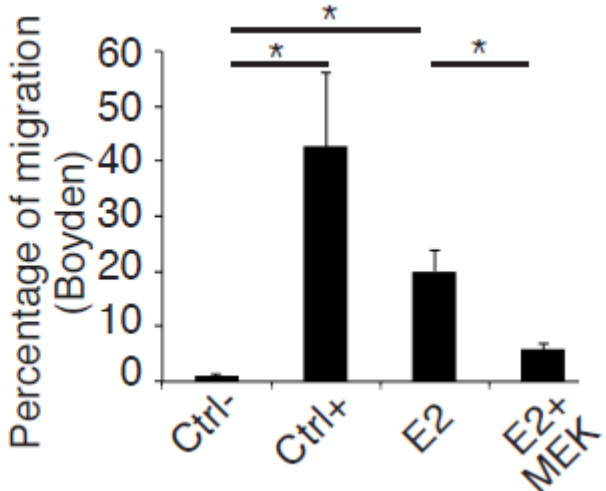
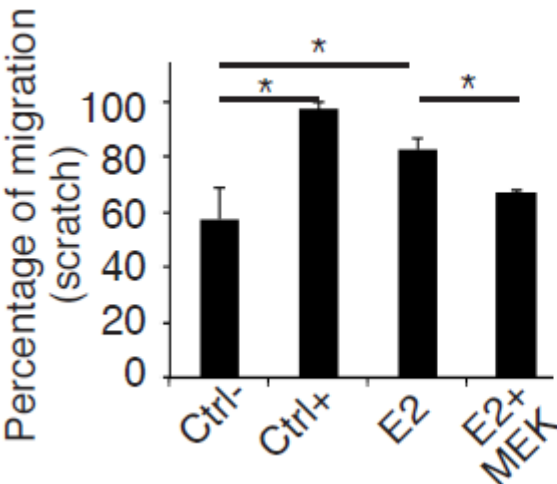
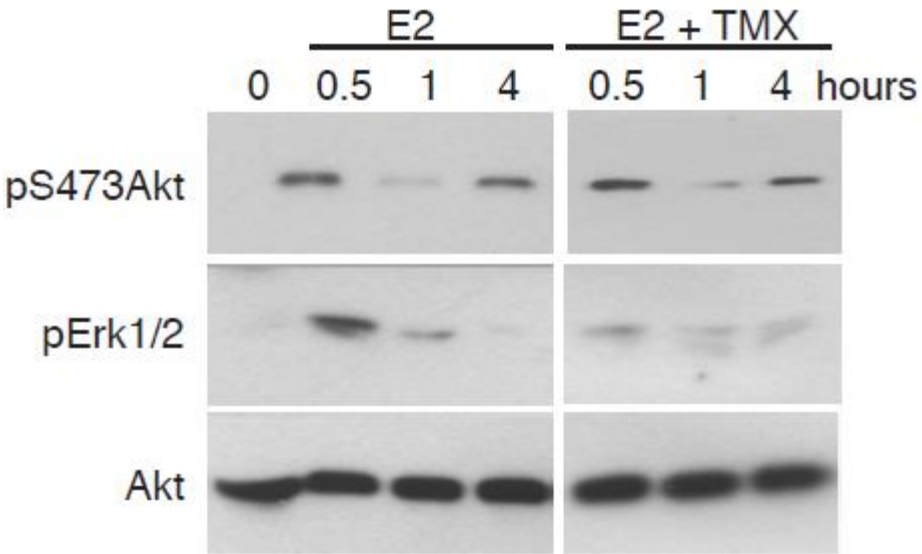
# Tamoxifen inhibits beneficial effects of estradiol



# Tamoxifen inhibits lymphatic endothelial cells functions



# Tamoxifen effects are mediated through pERK pathway.



# Acknowledgements

**I2MC UMR 1048**

**Team 15**

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