



# *Project BASTION „From Basic to Translational Research in Oncology”*

## **Kick-off Meeting International Advisory Board Meeting**

**Warsaw**

November 27th 2012





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Department of Histology  
and Embryology



# Research interests

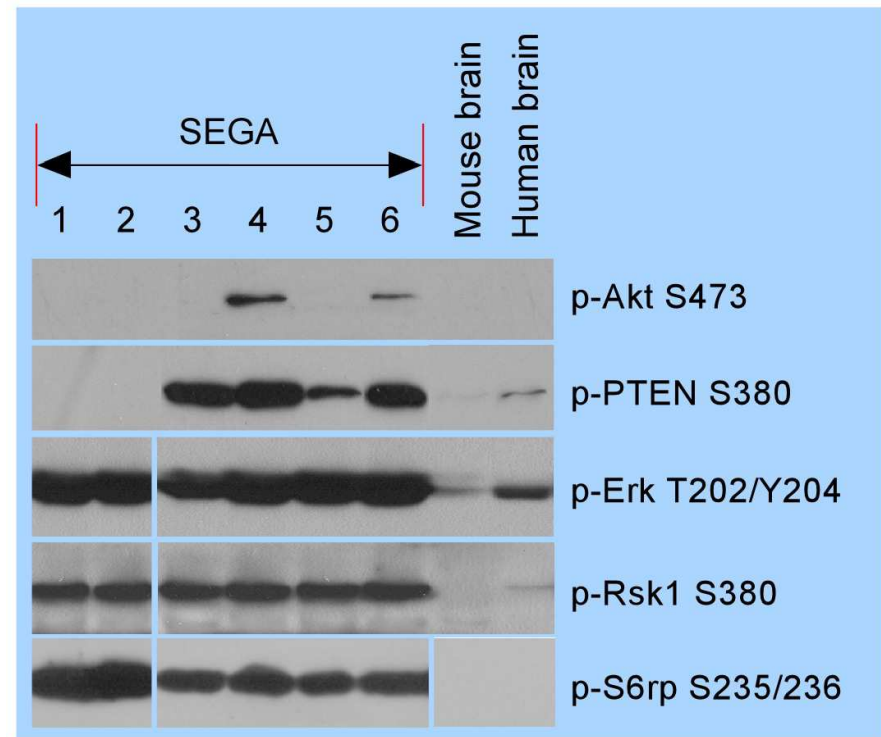
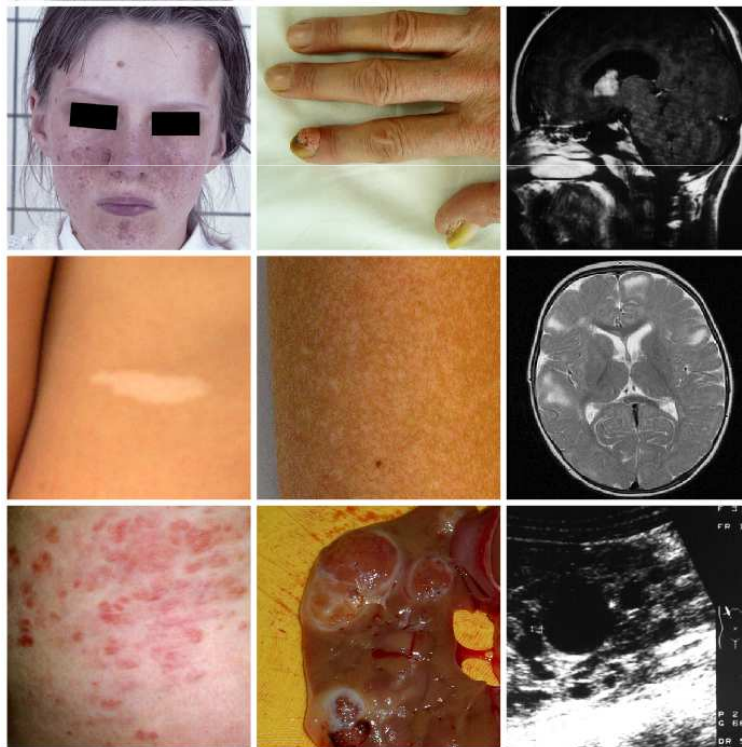
- mTOR signaling in leukemia and neuropathology
- miRNAs regulating the expression of inhibitors of MMPs in prostate cancer and bladder cancer
- Epigenetic regulation of TIMPs in endometriosis
- SNPs that predict recurrent hepatitis C in liver transplants

# mTOR signaling in leukemia and neuropathology

- CML
  - Potential target for augmentation of TKI
- Tuberosclerosis
  - SEGA tumors development – haploinsufficiency or postranslational modifications?
- Pituitary adenomas
  - Mechanism of mTOR hyperactivation in GHomas

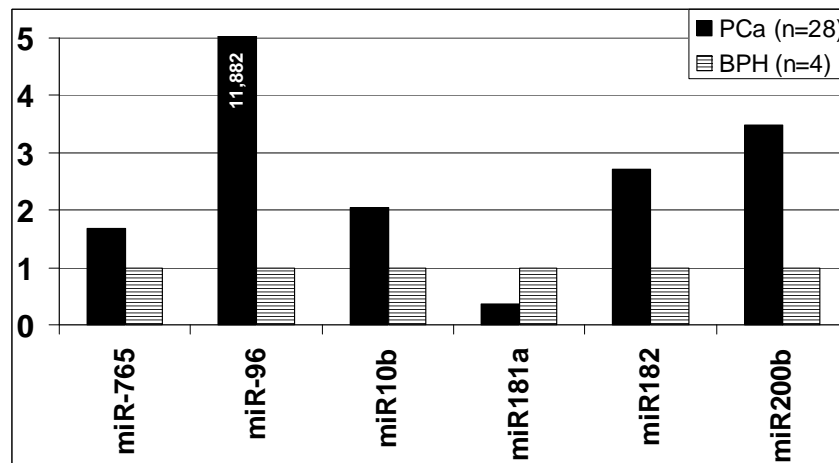
*Tomasz Stokłosa, M.D., PhD*  
*Jarosław Józwiak, M.D., PhD*  
*Emir Ahmed Sajjad, M.D.*

# Tuberous sclerosis



# miRNAs regulating inhibitors of MMPs in prostate cancer

- miRNAs predicted to regulate TIMP1-4
- TIMP1-4 expression in cancer tissue



Spearman's rank correlation coefficient CaP (n=28)

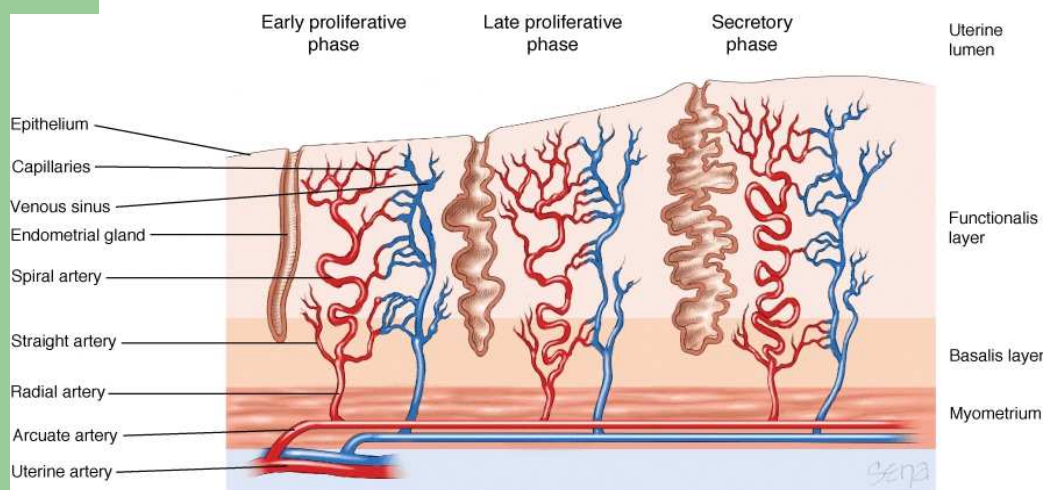
| Gene  | microRNA | R      |
|-------|----------|--------|
| TIMP2 | miR-200b | 0.31   |
|       | miR-10b  | -0.01  |
| TIMP3 | miR-10b  | 0.21   |
|       | miR-181a | 0.37   |
|       | miR-765  | 0.38   |
| TIMP4 | miR-96   | -0.015 |
|       | miR-10b  | 0.57   |
|       | miR-200b | 0.58   |
| RECK  | miR-200b | 0.07   |
|       | miR-181a | 0.14   |
|       | miR-765  | -0.03  |
|       | miR-182  | -0.007 |
|       | miR-10b  | -0.15  |

# Epigenetic regulation of TIMPs in endometriosis

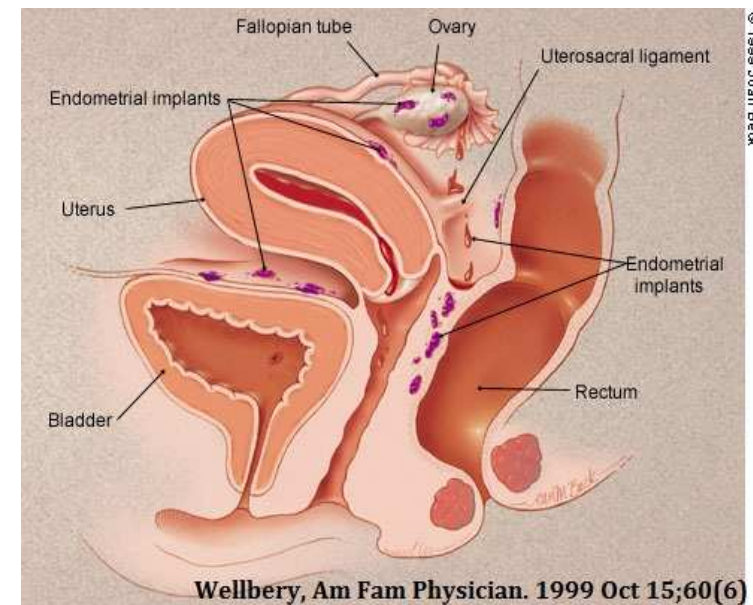
- miRNAs predicted to regulate TIMP2-4 and Reck
- TIMP2-4 and Reck expression in eutopic and ectopic endometrium
- miRNA profile differ between eutopic and ectopic tissue
- The role of hypoxia - induction of miRNA expression

# Endometriosis

- Endometriosis - hormone dependent disorder characterized by growth of endometrial tissue outside uterine cavity.

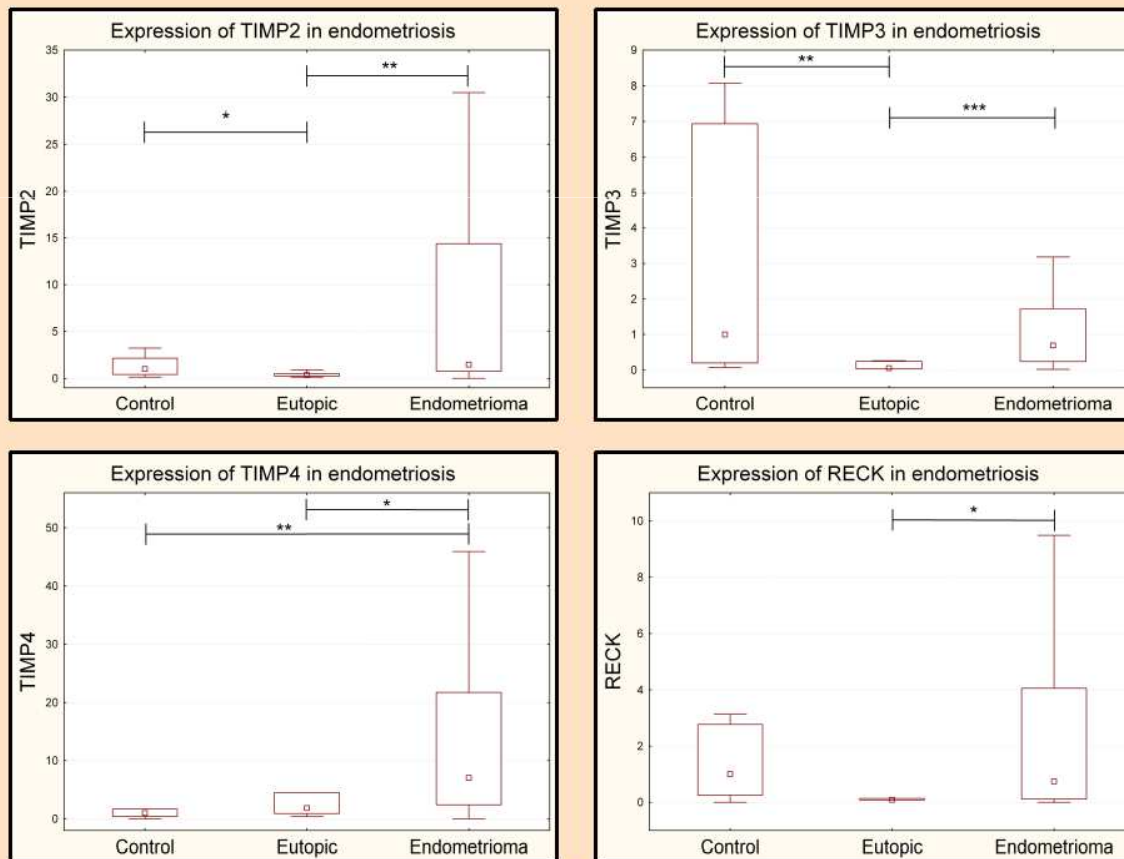


Source: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY: *Williams Obstetrics, 23rd Edition*: <http://www.accessmedicine.com>





# Expression of TIMP/RECK in biopsies

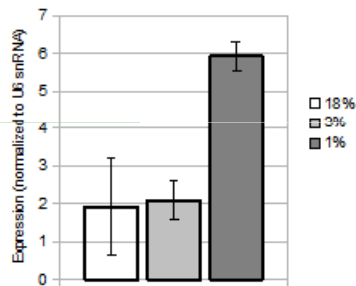


p-value thresholds: <.05(\*), <.01(\*\*), <.001(\*\*\*)

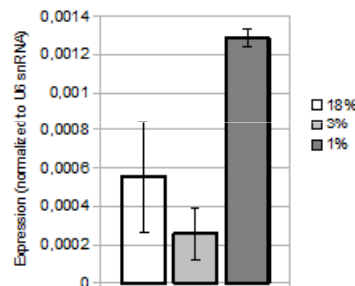
*Radosław Maksym, M.D.*

# The role of hypoxia - induction of miRNA expression

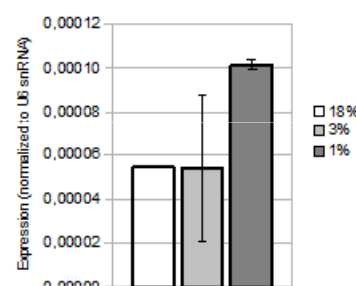
Ze750e11 - miR21 in hypoxia 48h



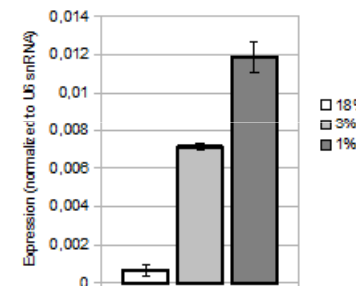
Ze750e11 - miR-182 in hypoxia



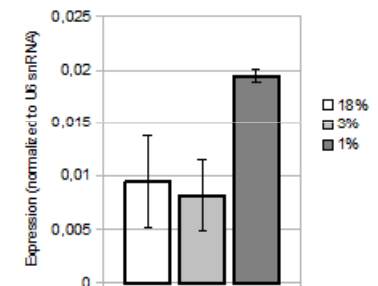
Ze750e11 - miR-200b in hypoxia



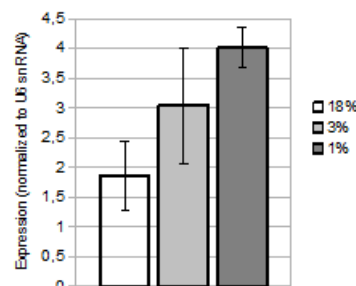
Ze750e11 - miR210 in hypoxia



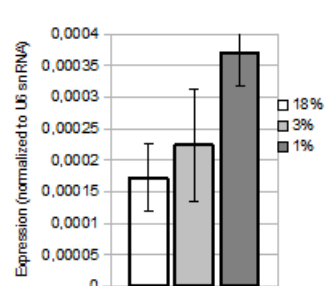
Ze750e11 - let-7f in hypoxia



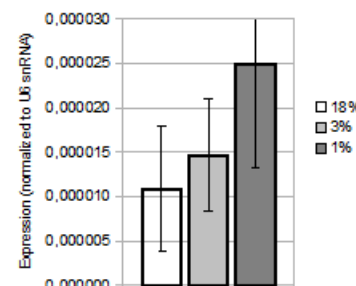
Ze650g12 - miR21 in hypoxia 48h



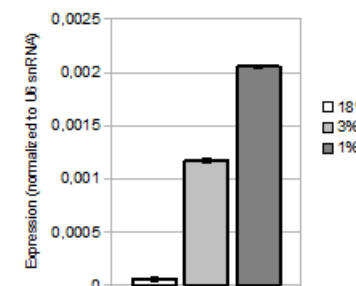
Ze650g12 - miR-182 in hypoxia 48h



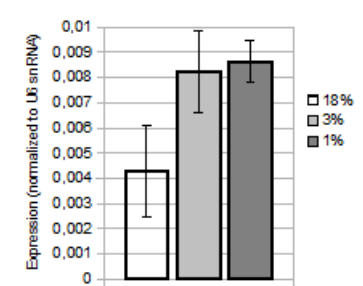
Ze650g12 - miR-200b in hypoxia 48h



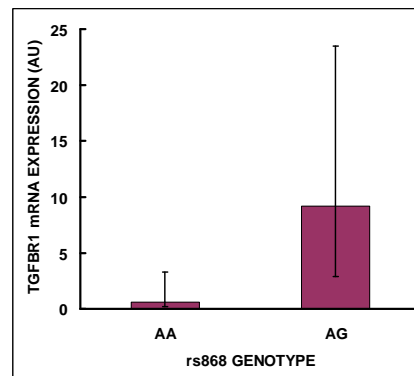
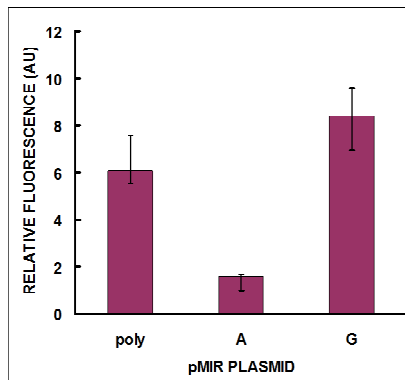
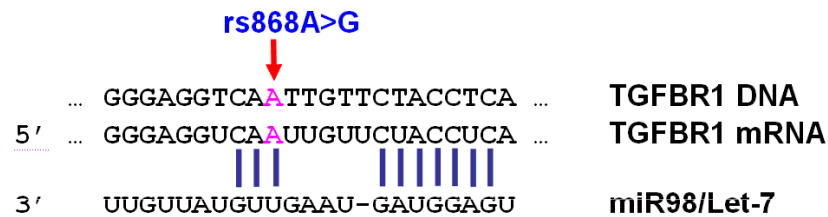
Ze650g12 - miR210 in hypoxia 48h



Ze650g12 - let-7f in hypoxia 48h



# SNPs in that predict recurrent hepatitis C in liver transplants



- Allel A rs868 correlates with poorer prognosis in HCV+ liver graft recipients
- Allel A correlates with lower expression of TGFBR1

Remains to be determined:

- Role of SNP rs868 in HCV-liver transplants