Labmeeting

20120703

- Schematic illustrate the signaling events after the angiotensin stimulation

Angiotensin

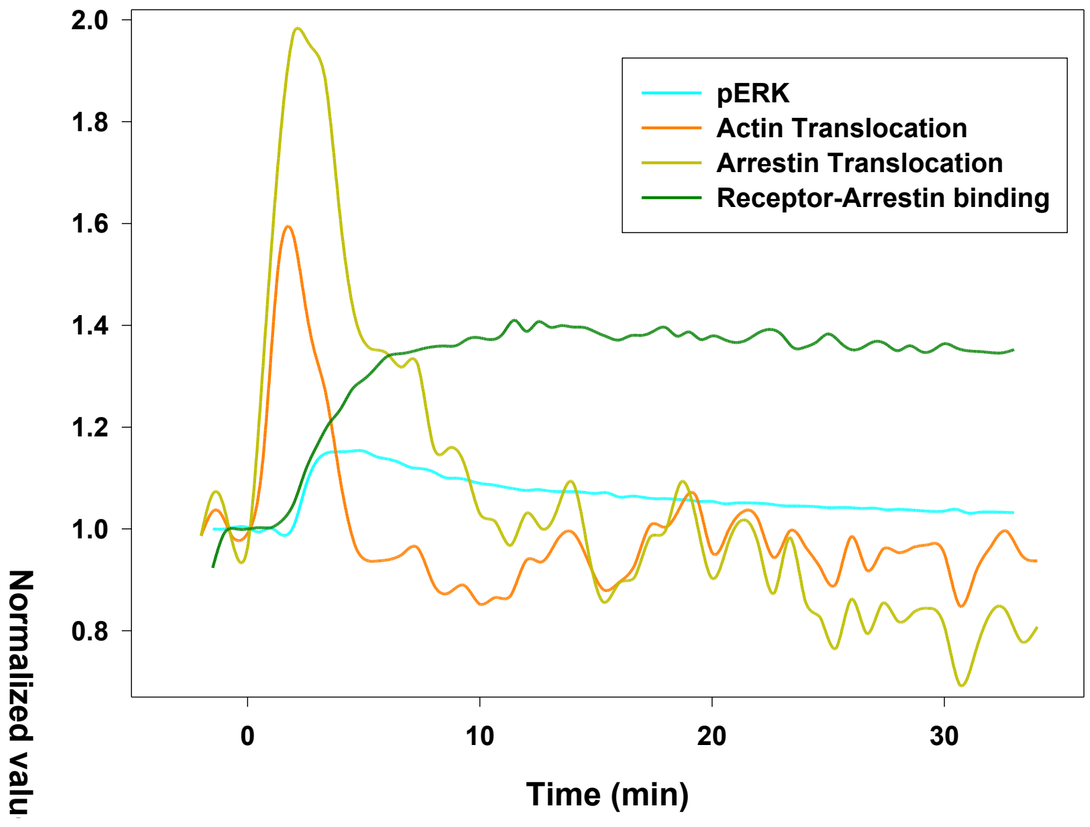
Angiotensin Receptor

β-arrestin

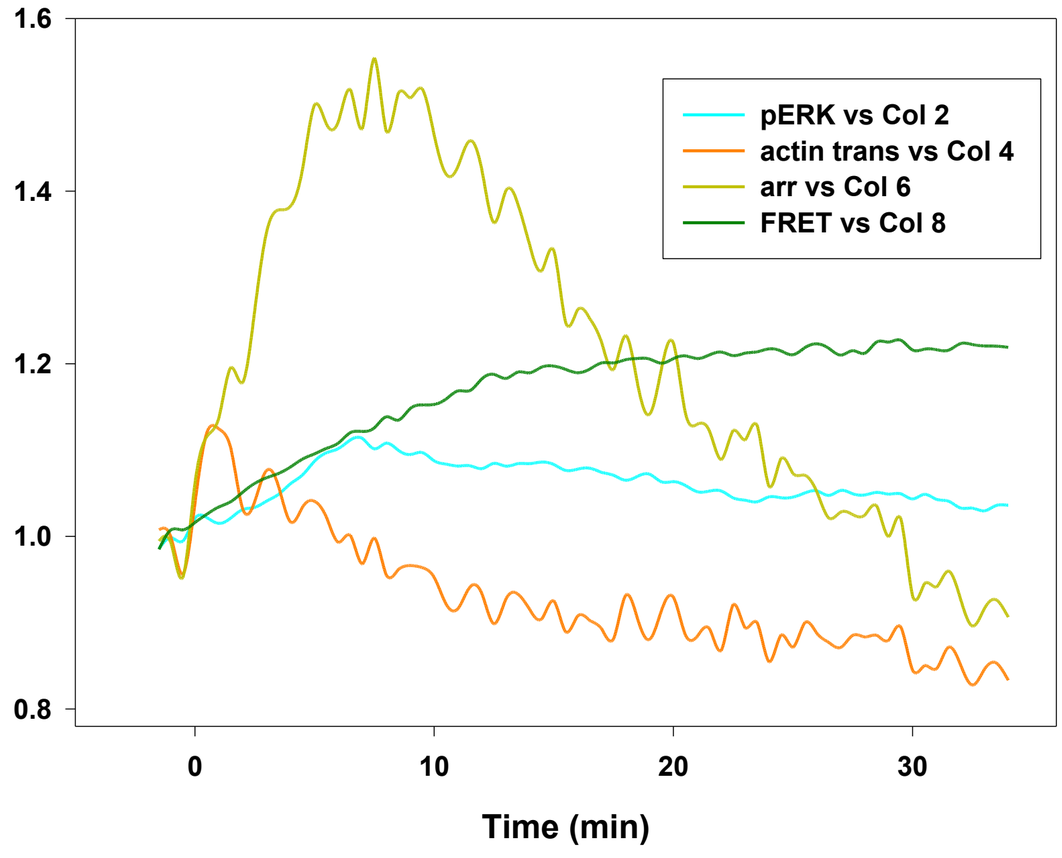
MAPK cascade

Cytoskeleton

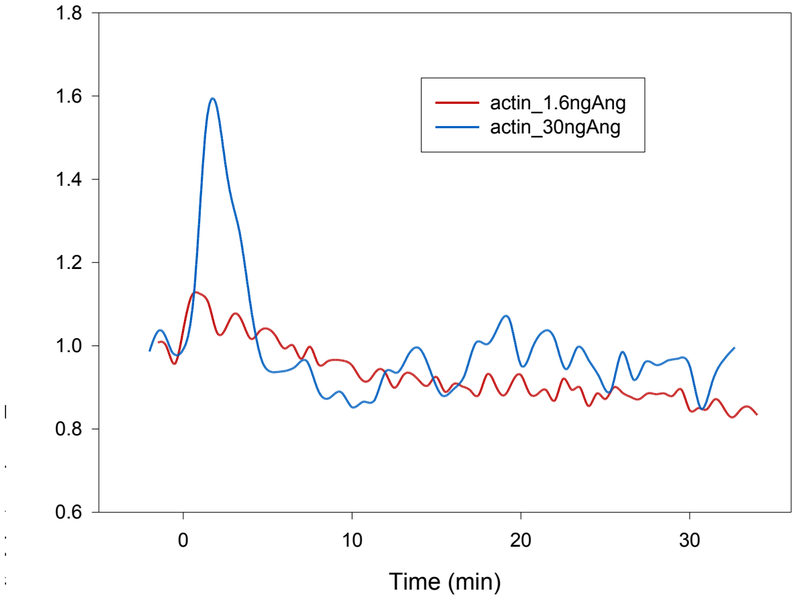
Signaling Events at 30ng Ang



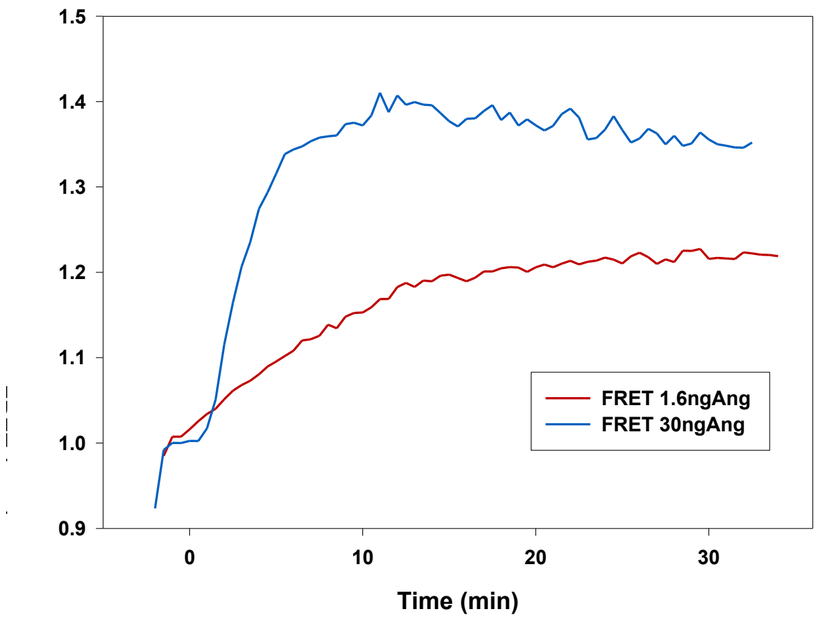
sequence of events at 1.6ngAng



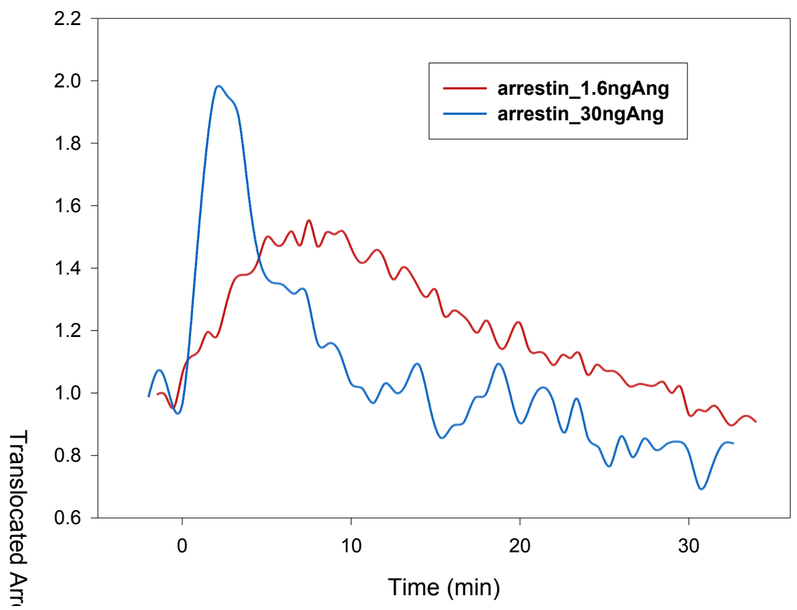
Actin Translocation to the membrane



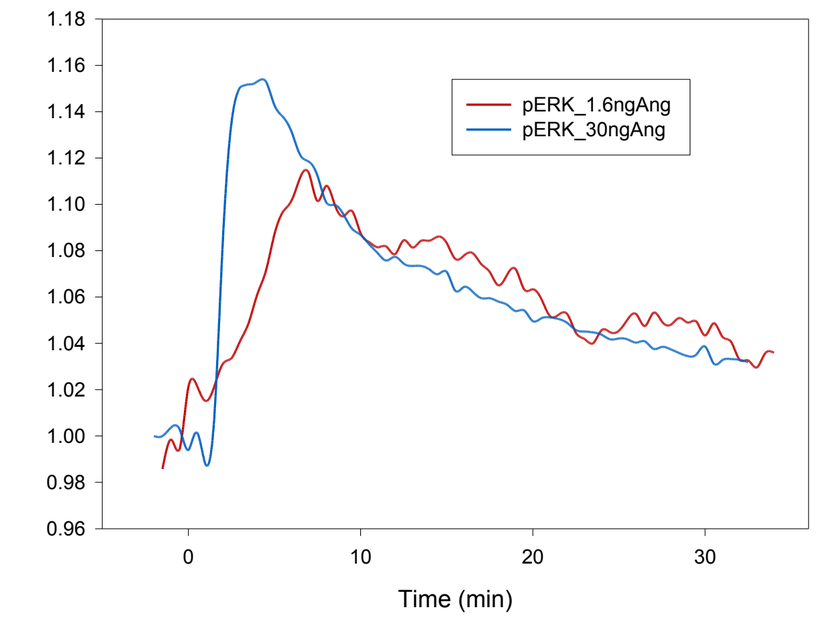
Receptor-arrestin FRET



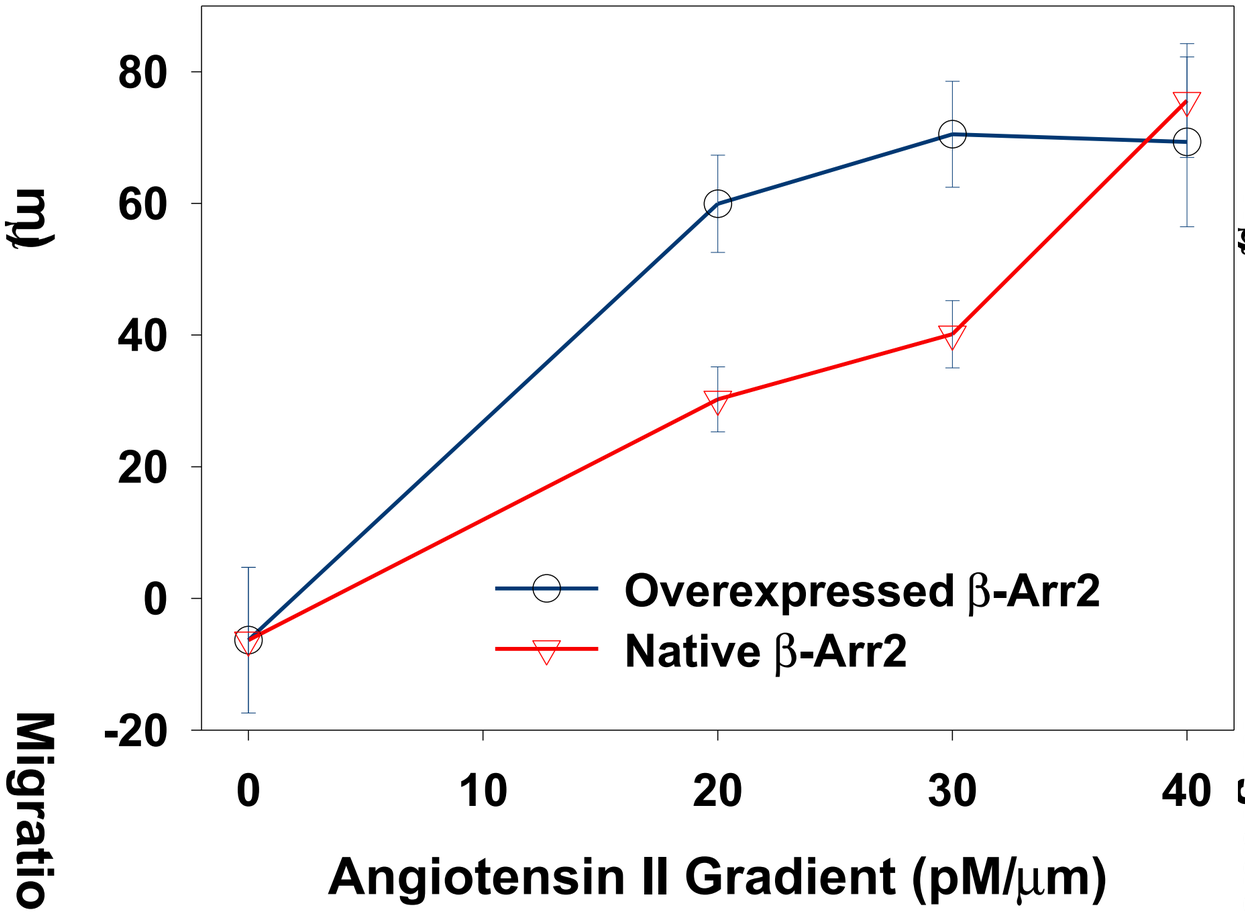
Arrestin Translocation to the membrane

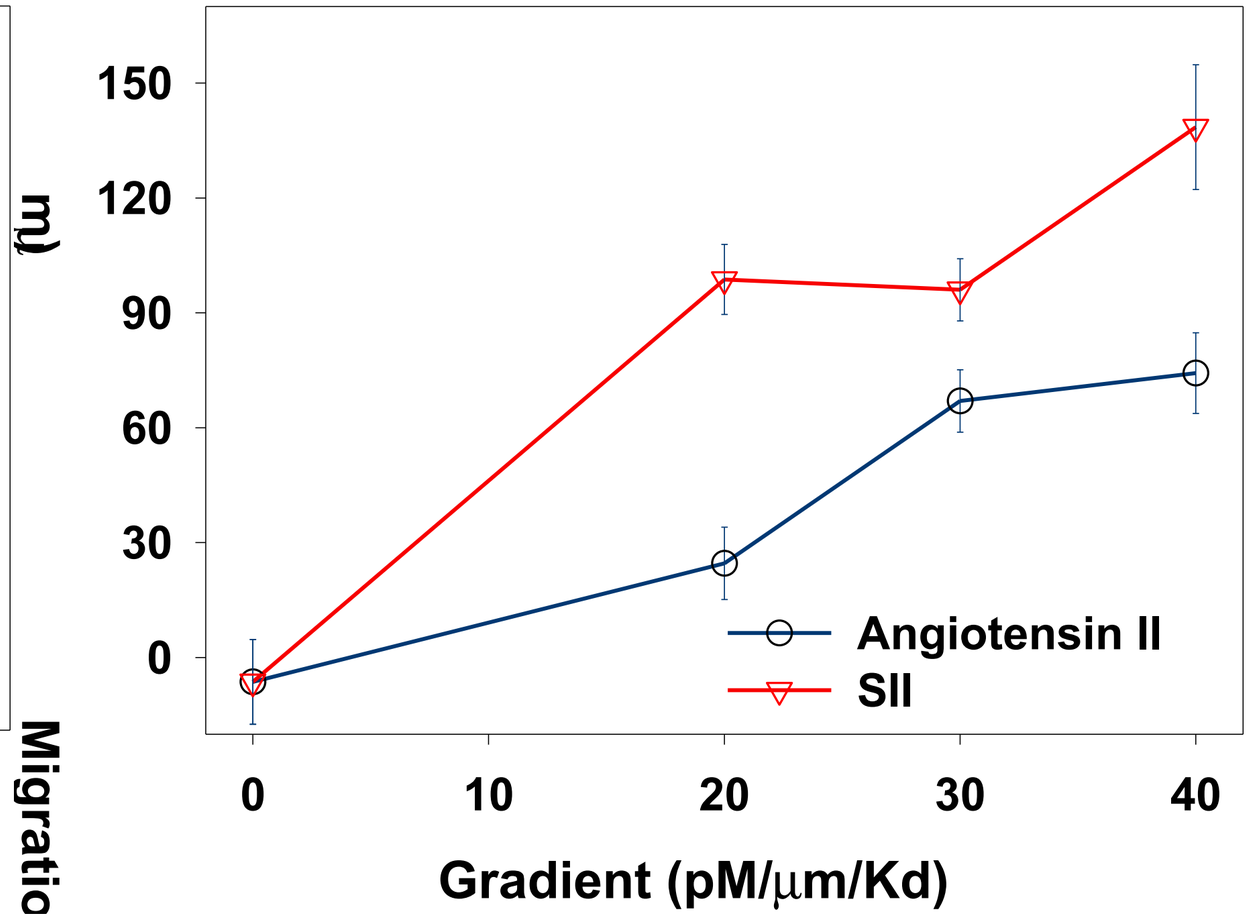


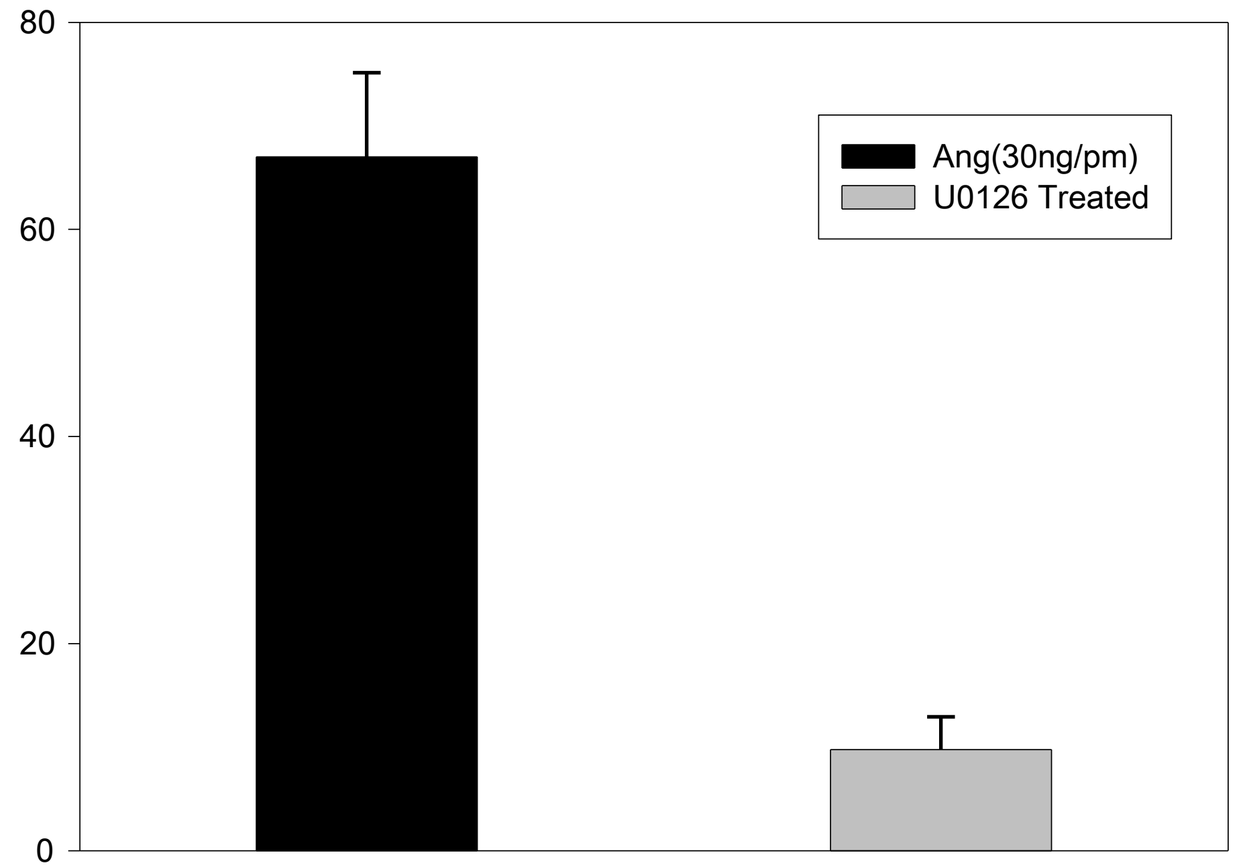
pERK activation

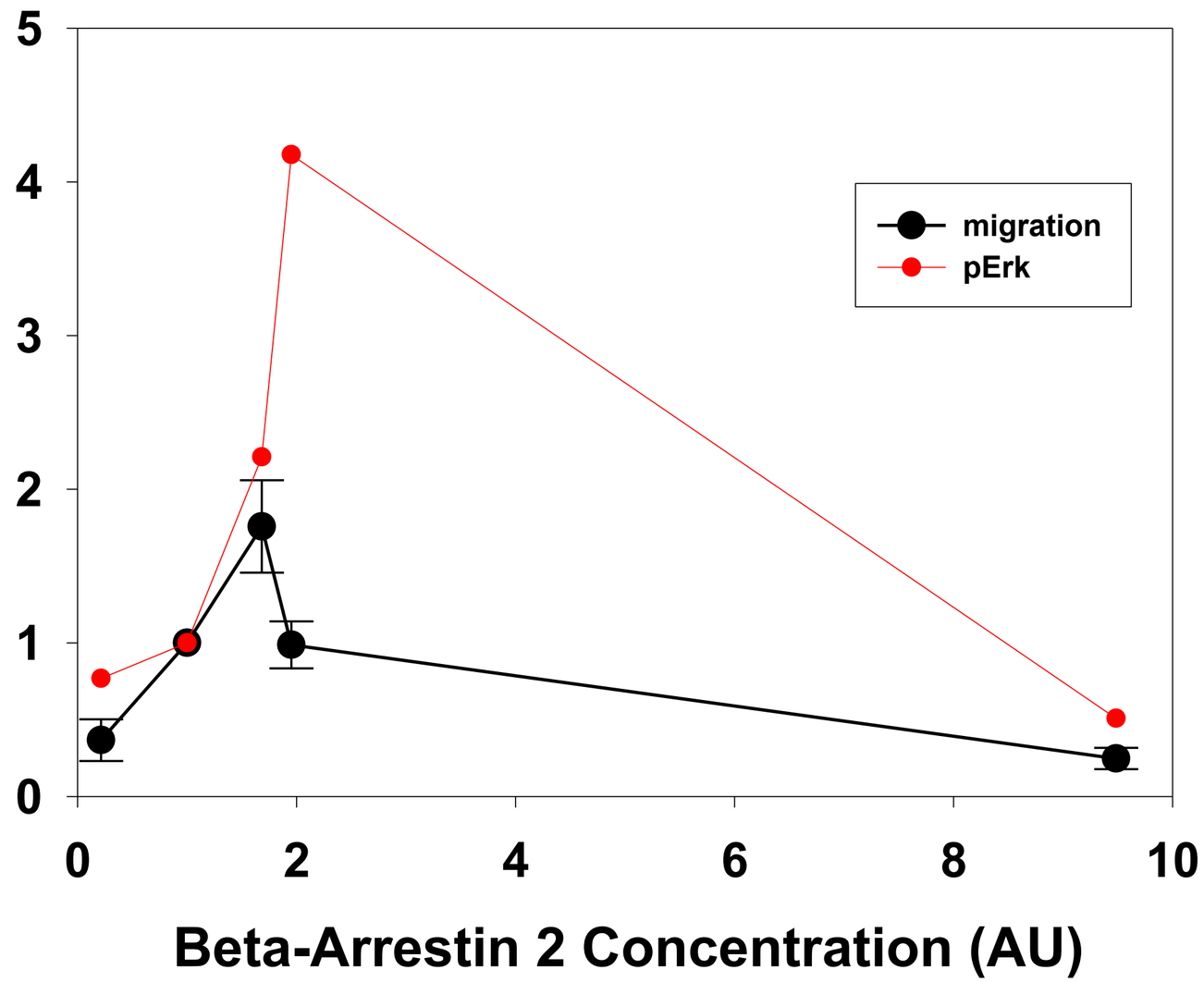


- Cell chemotaxis to angiotensin gradient is depand on the gradient, arrestin concentration and the ligands

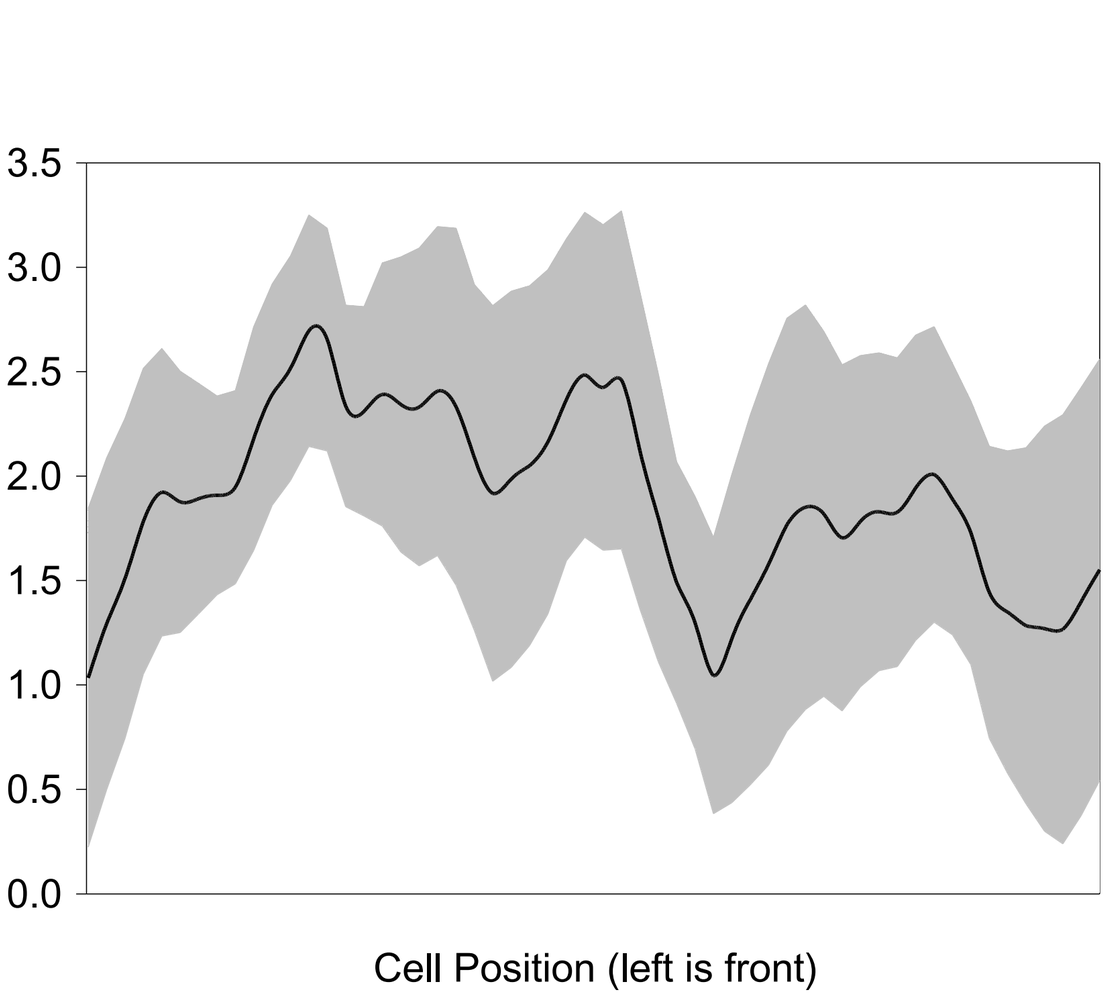

80
60
40
20
0
-20
0
10
20
30
40
Overexpressed β-Arr2
Native β-Arr2
Angiotensin II Gradient (pM/μm)
Migratio

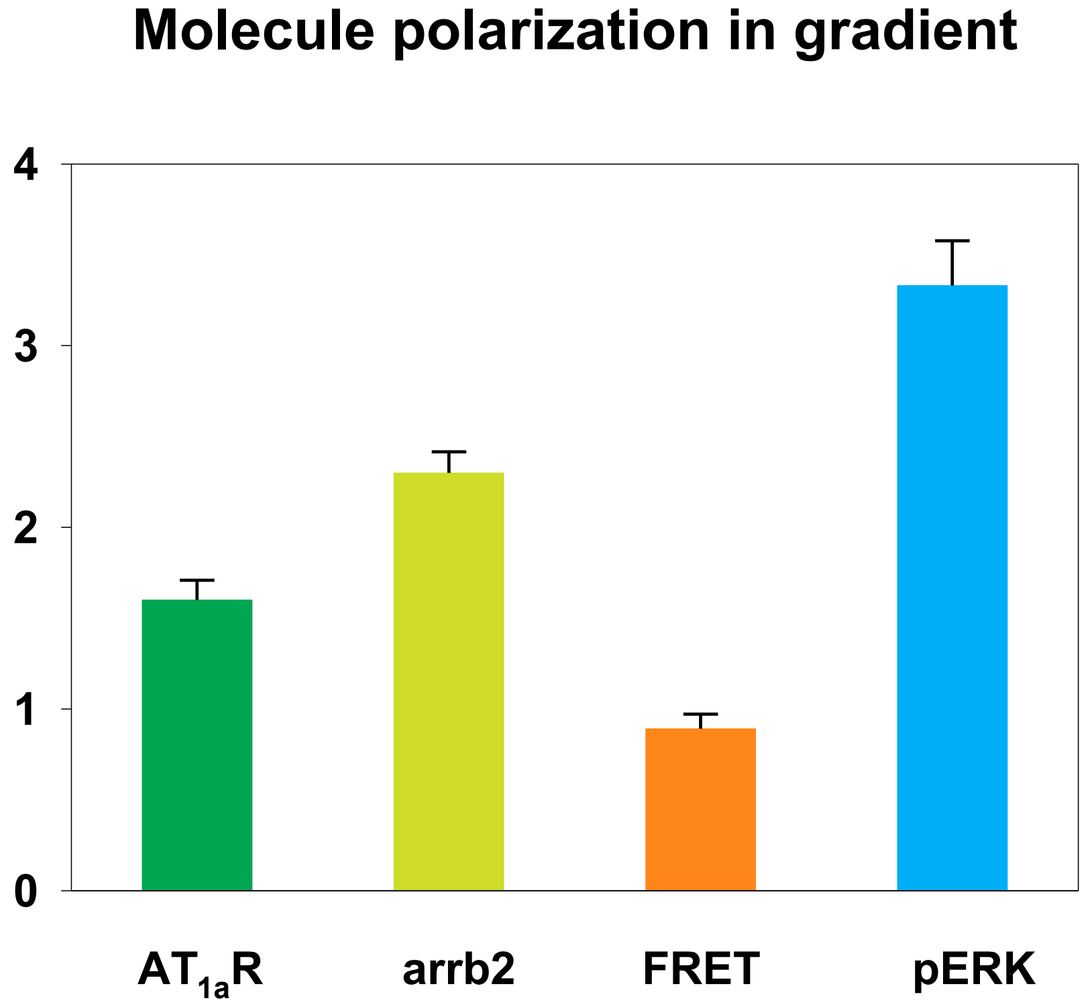

150
120
90
60
30
0
0
10
20
30
40
Angiotensin II
SII
Gradient (pM/μm/Kd)
Migratio


U0126 inhibits the chemotaxis
80
60
40
20
0
Ang(30ng/pm)
U0126 Treated

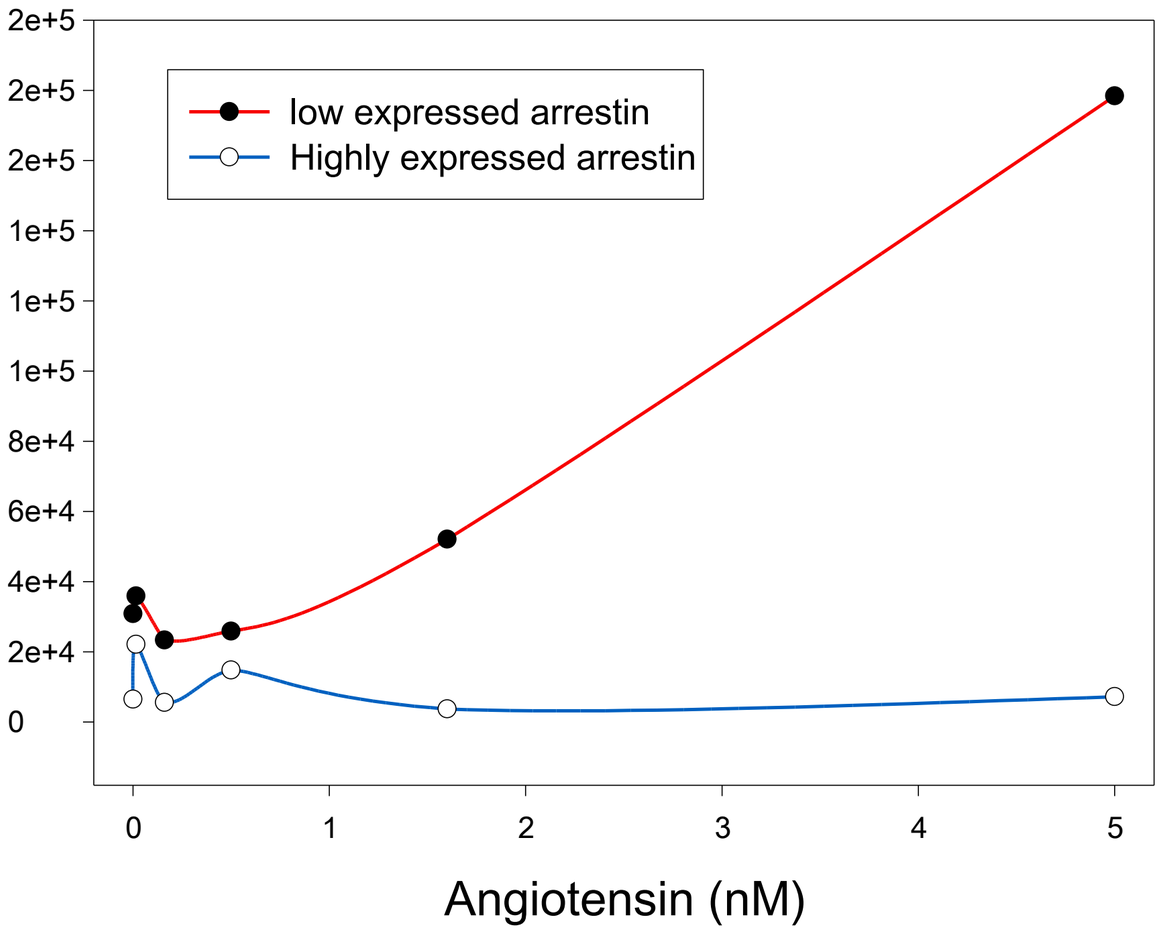

5
4
3
2
1
0
0
2
4
6
8
10
migration
pErk
Beta-Arrestin 2 Concentration (AU)

- During the signal transduction, the polarizations of signals are amplified step-by-step.

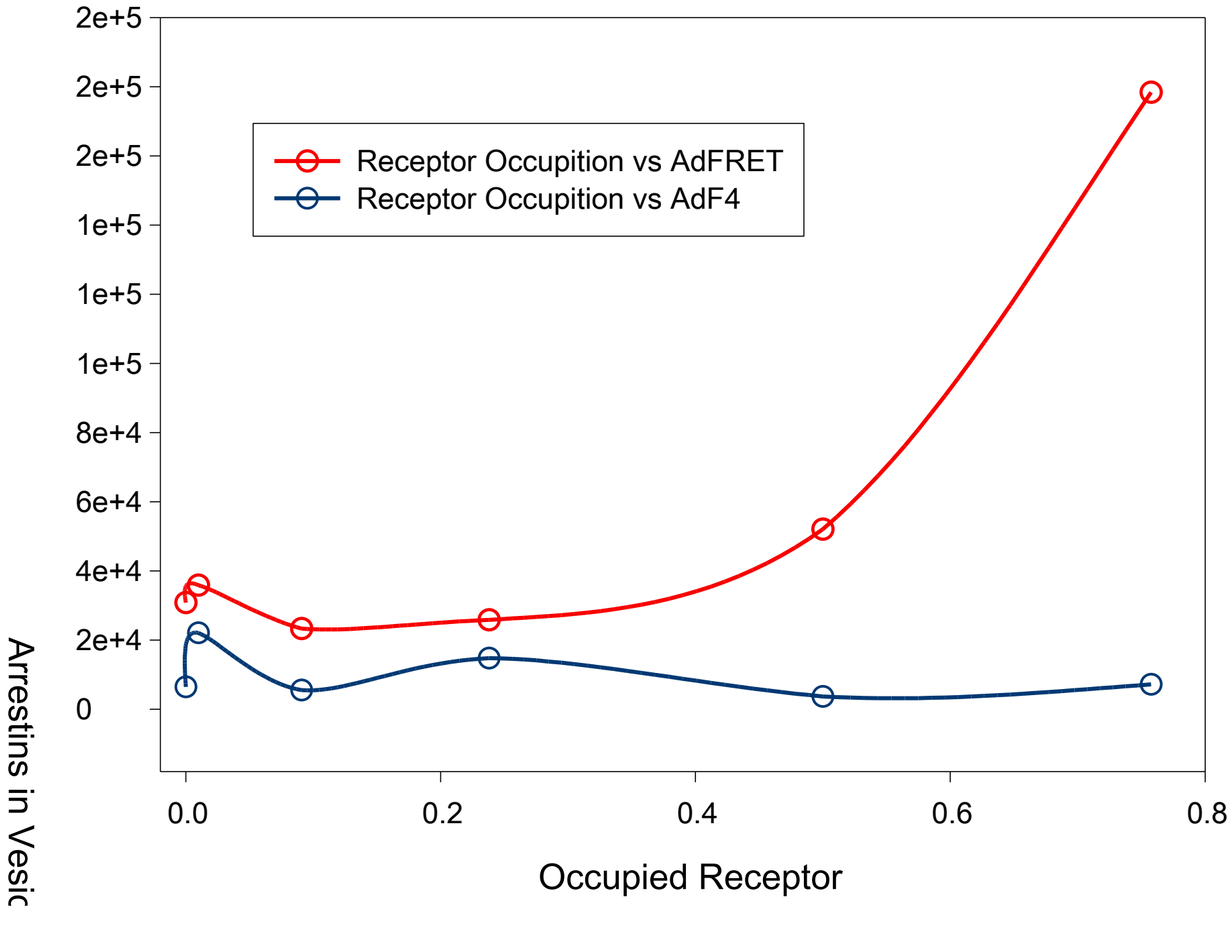

3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Cell Position (left is front)


Molecule polarization in gradient
4
3
2
1
0
AT1aR
arrb2
FRET
pERK

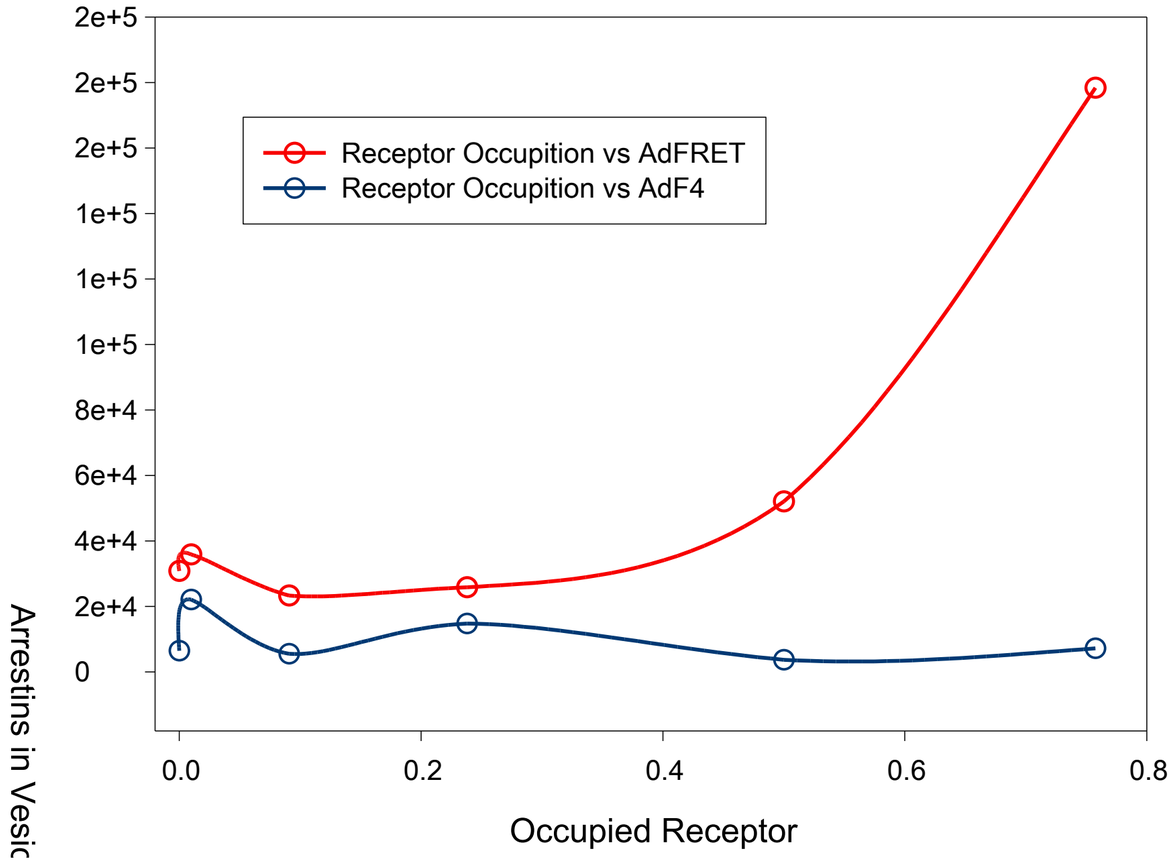
Arrestin inside vesicles

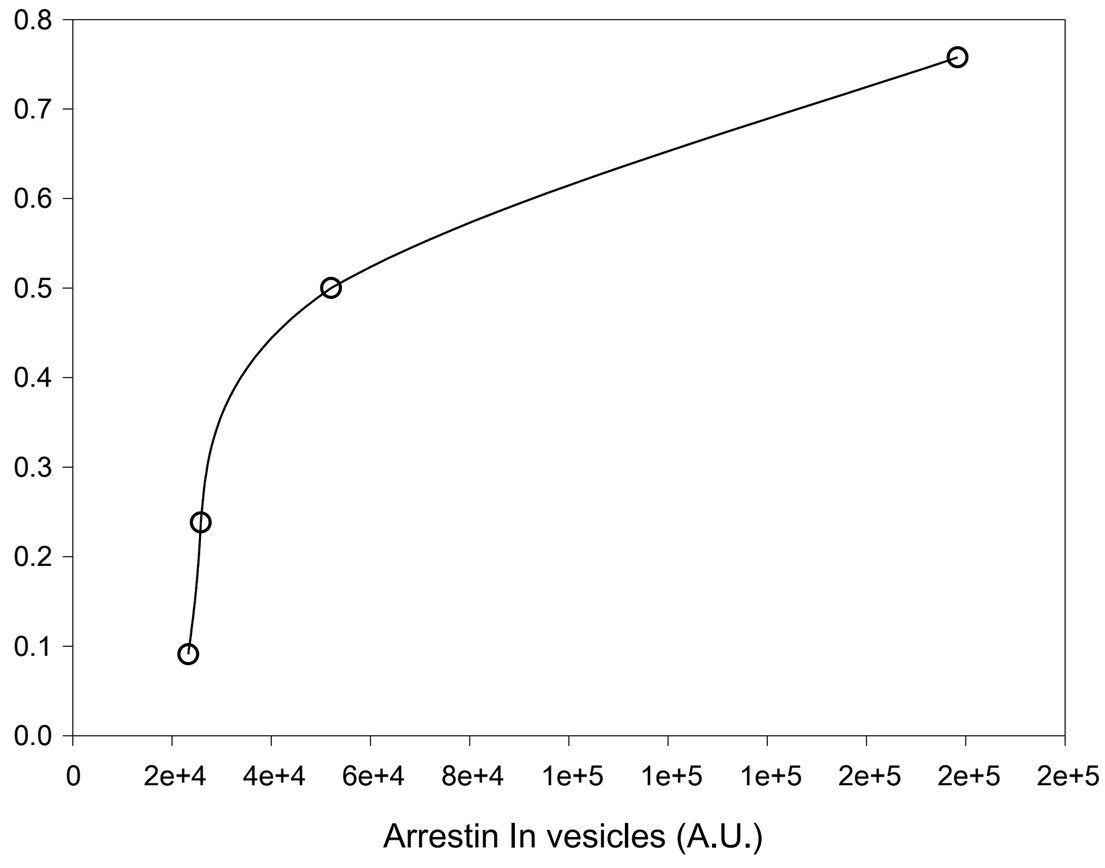


Arrestin inside vesicles



Arrestin inside vesicles

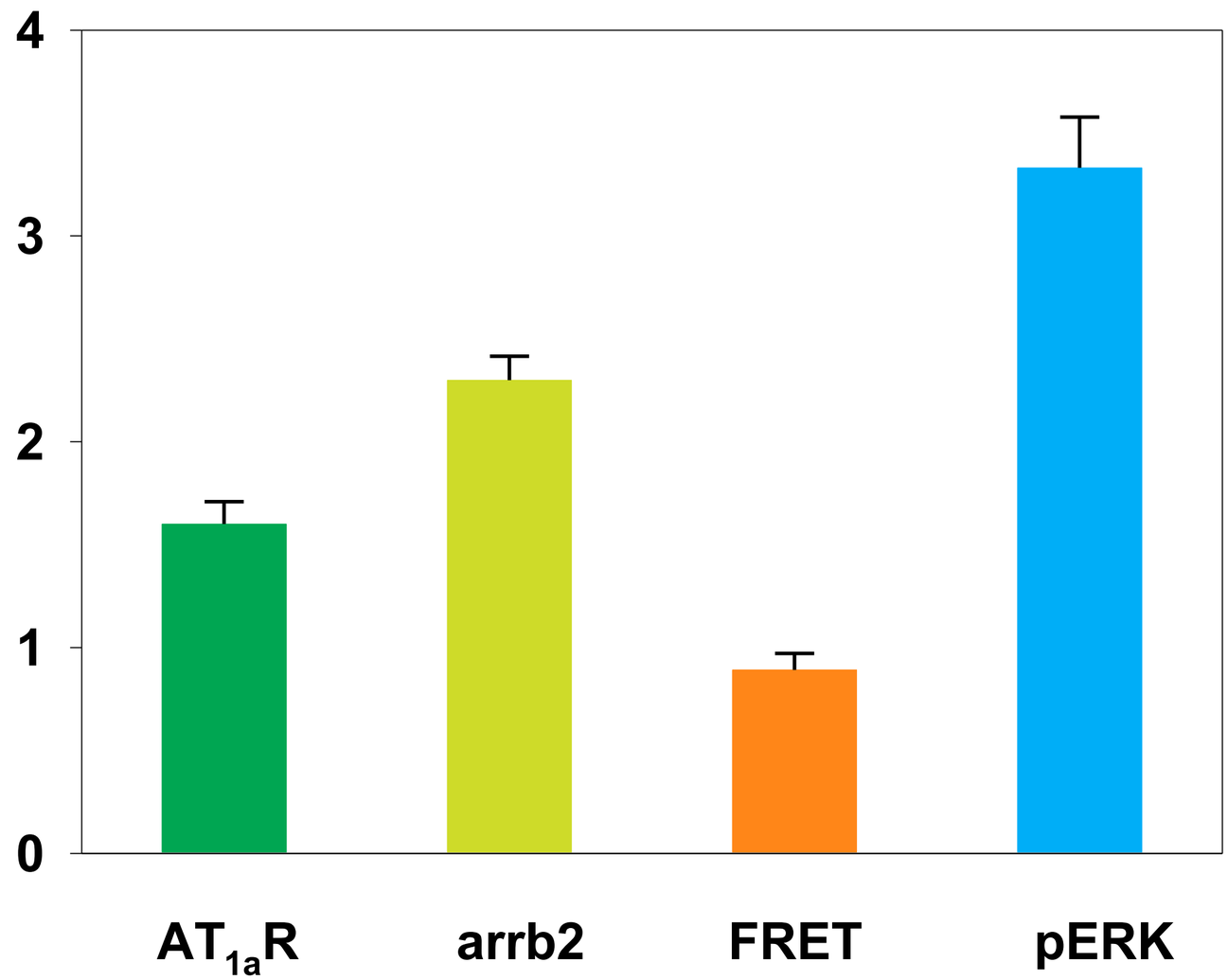




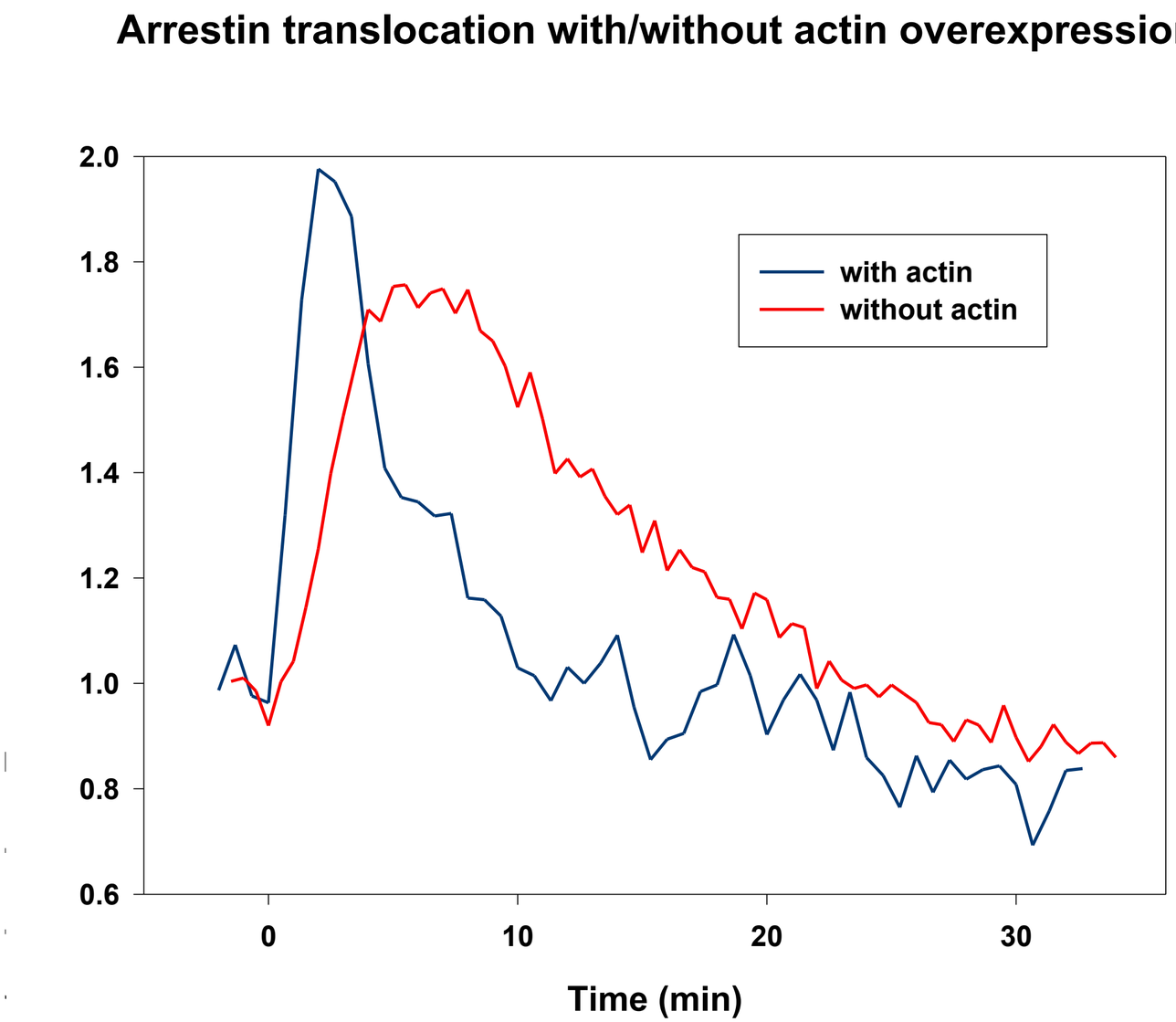
$$occupied\_receptor = \frac{Arrestin}{Arrestin + 27500}$$

$$R^2 = 0.97$$

Molecule polarization in gradient



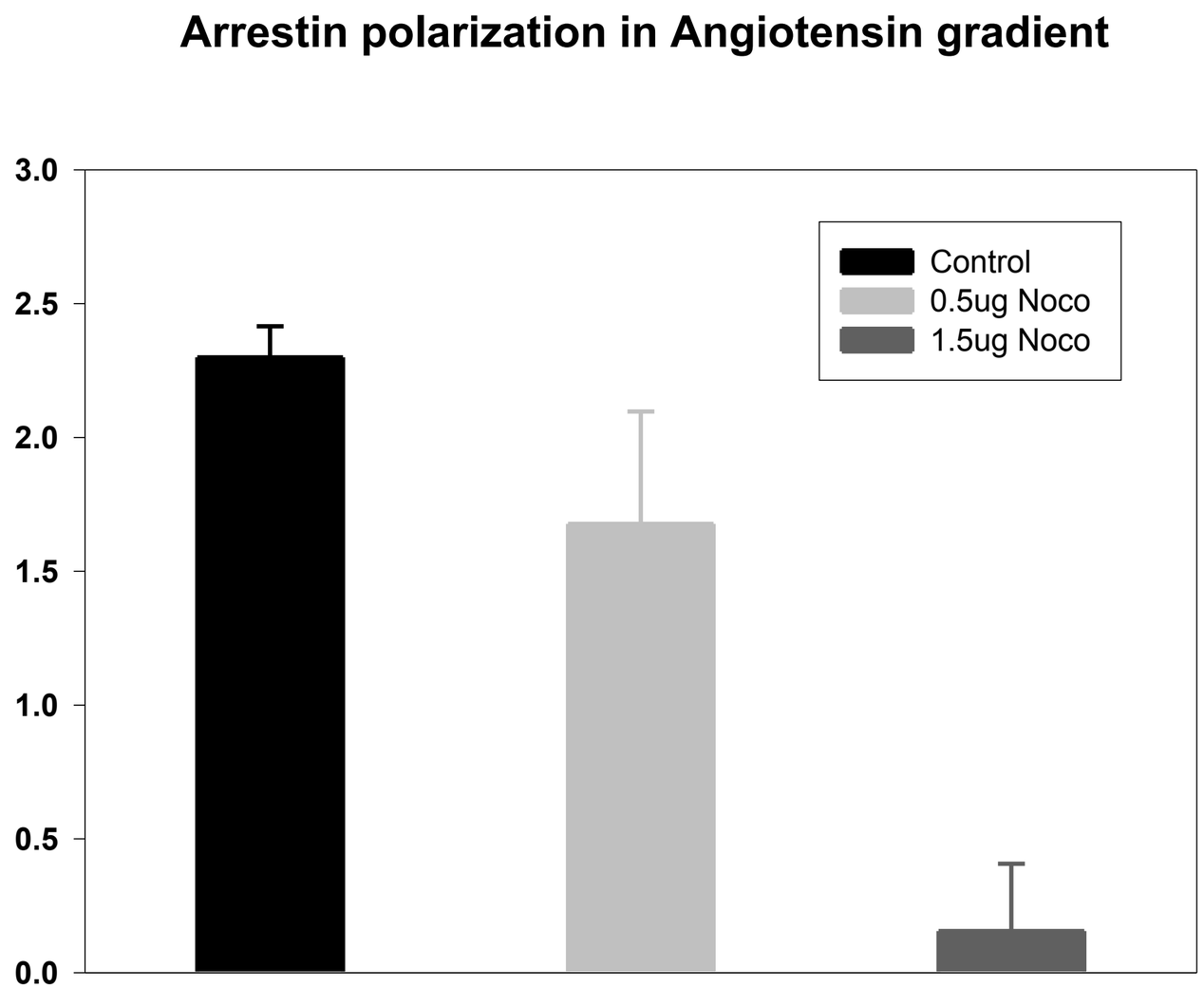
Actin effect on arrestin translocation



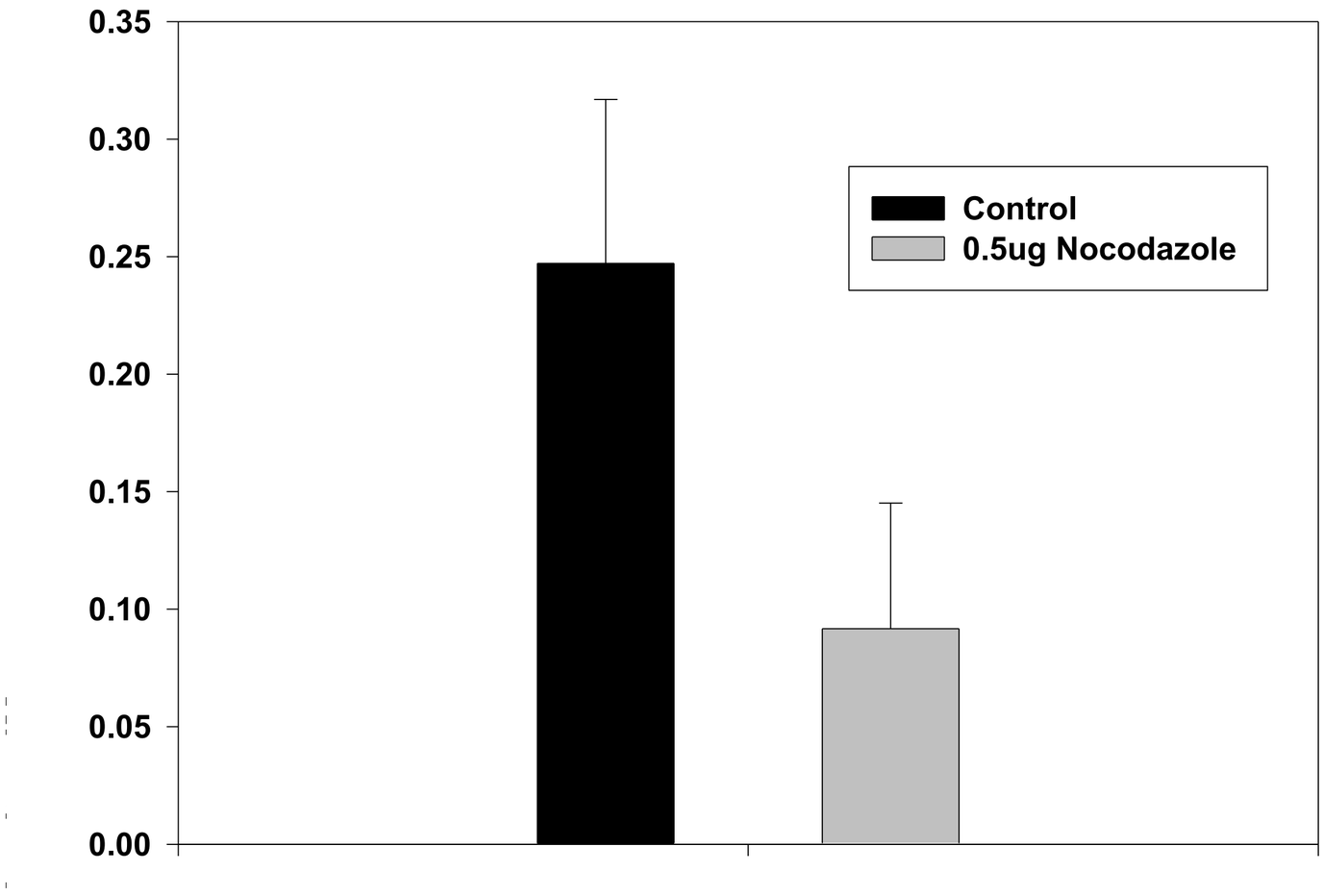
Control

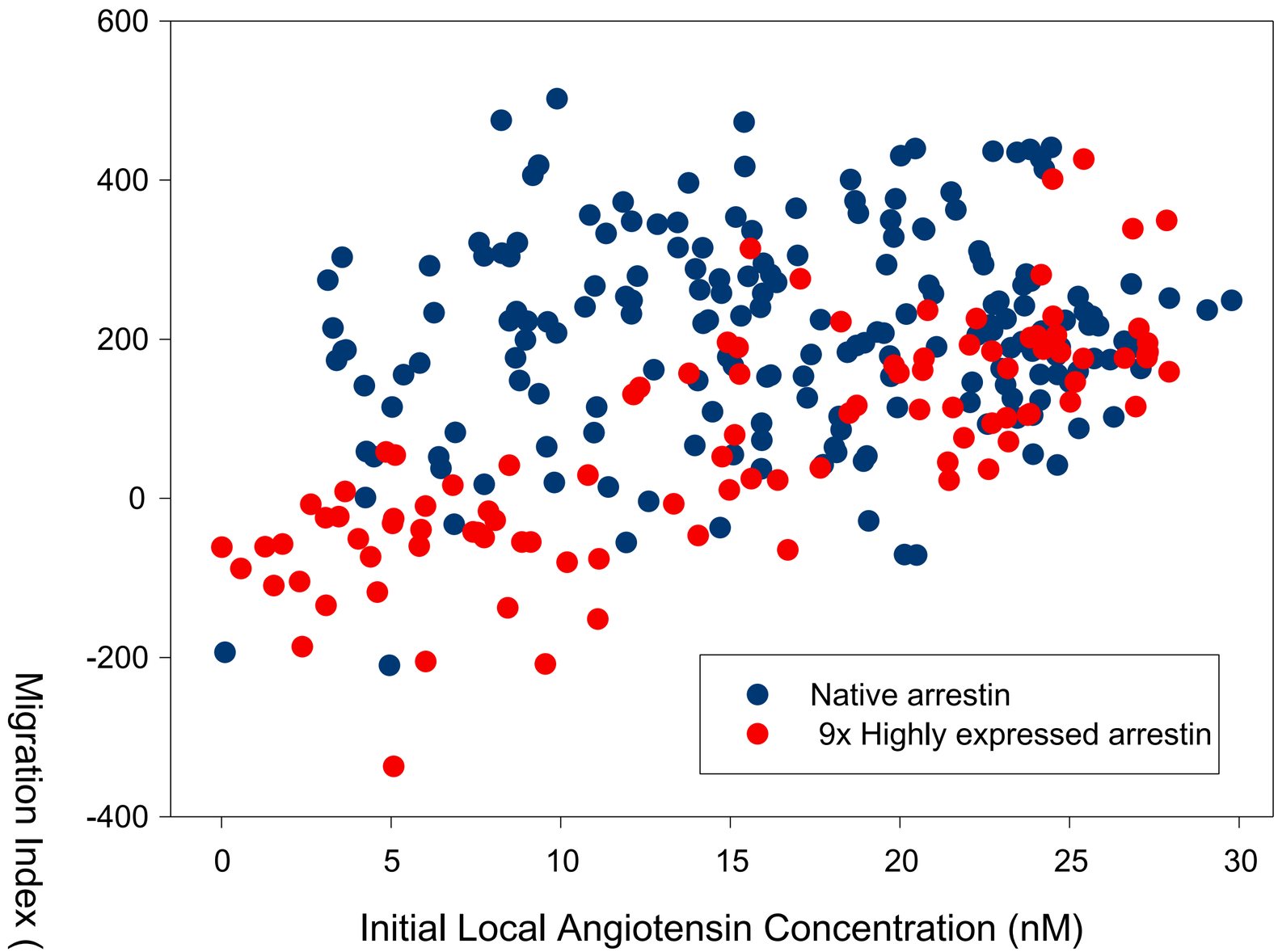
Nocodazole treat

Nocodazole inhibit the microtubule and arrestin polarization

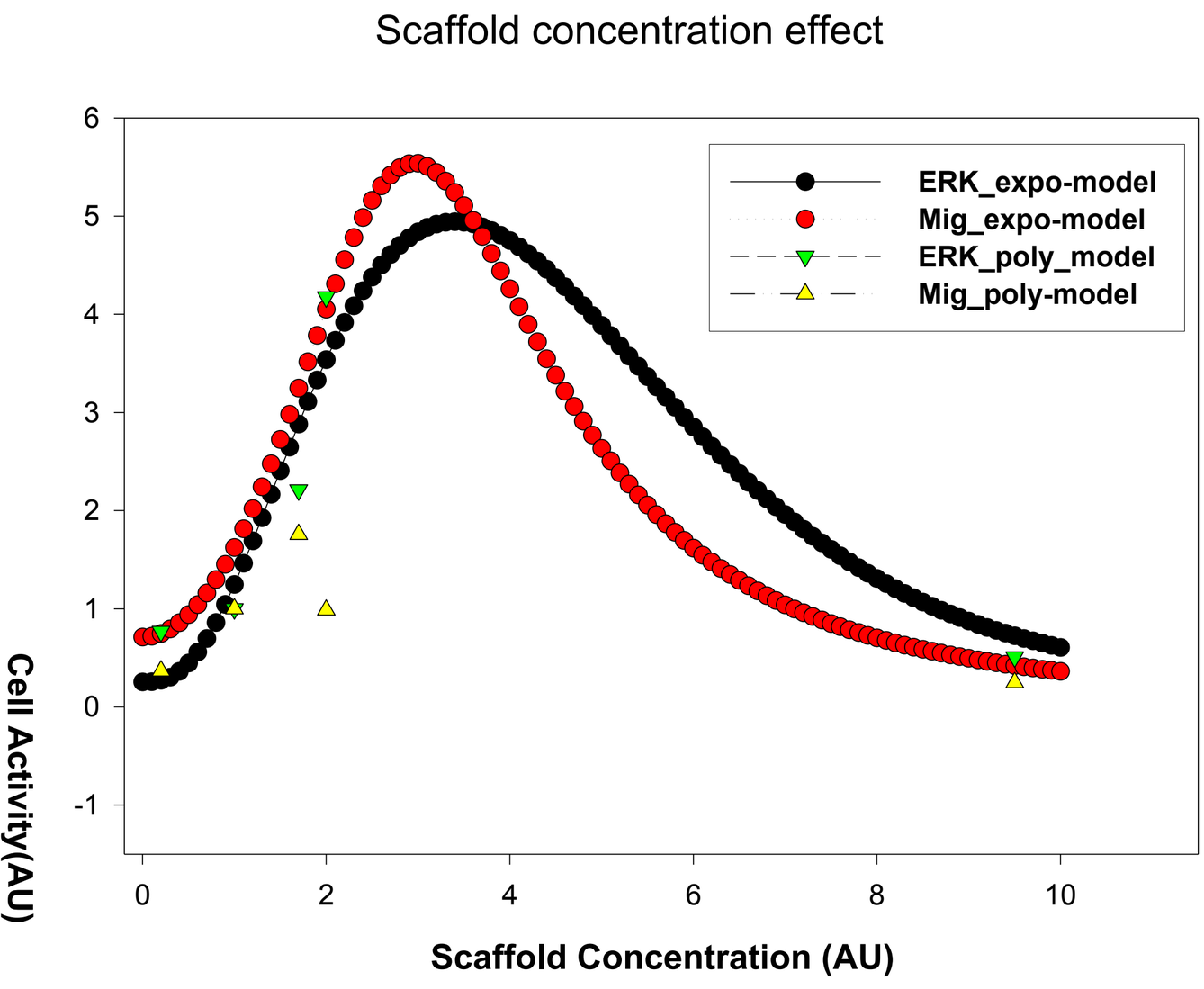


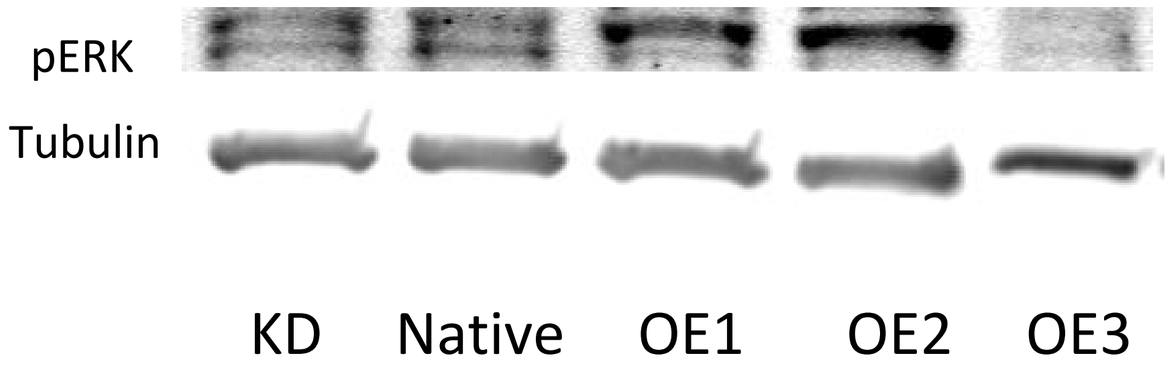
Highly expressed arrestin

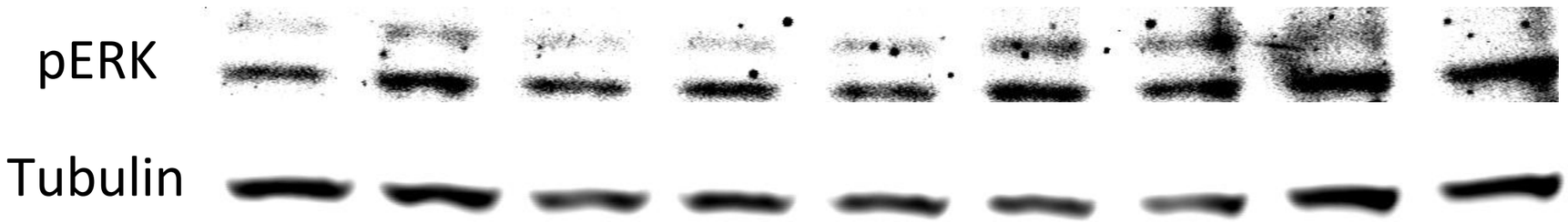



600
400
200
0
-200
-400
0
5
10
15
20
25
30
Migration Index (
Initial Local Angiotensin Concentration (nM)
Native arrestin
9x Highly expressed arrestin

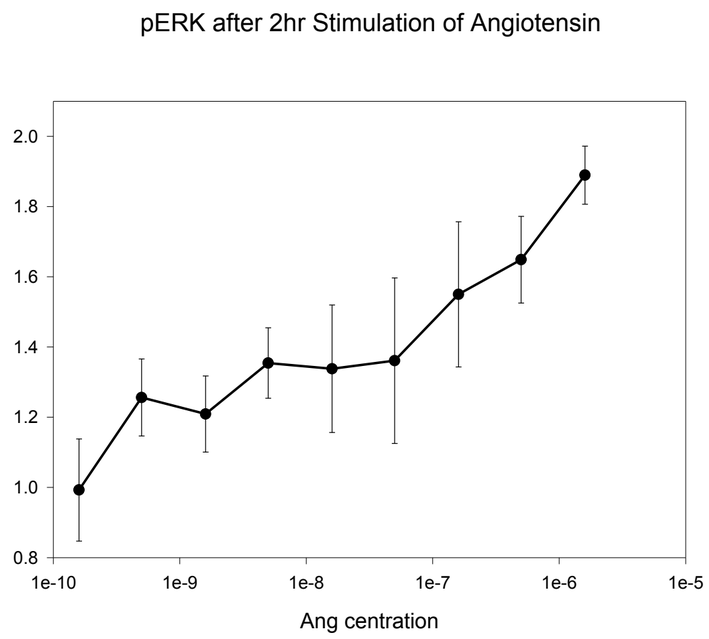
Thanks


Scaffold concentration effect
ERK_expo-model
Mig_expo-model
ERK_poly_model
Mig_poly-model
Cell Activity(AU)
Scaffold Concentration (AU)
6
5
4
3
2
1
0
-1
0
2
4
6
8
10


pERK
Tubulin
KD
Native
OE1
OE2
OE3



0.016ng 0.05ng 0.16ng 0.5ng 1.6ng 5ng 16ng 50ng 160ng



Reletive Actin Fluctuation VS Arrestin Concentration