Objectives: Resistance to endocrine therapy plays an important role in postmenopausal breast cancer therapy. Different mechanism(s) may be responsible, e.g. modulation of estrogen receptor-alpha (ERα). We could demonstrate that estradiol (E2)-induced proliferation of MCF-7 breast cancer cells overexpressing the progesterone receptor membrane component-1 (PGRMC1) was completely blocked by the selective estrogen receptor down-regulator (SERD) fulvestrant. In this project the response of MCF-7/PGRMC1 cells towards tamoxifen (Tam) was investigated.

Methods: Stable transfected MCF-7/PGRMC1-3HA cells were incubated with E2 (10-10 M) in the presence of Tam (10-9 to 10-6M) in various combinations - 'E2-first' or 'Tam-first' or both together ('continuously'). Proliferation rate was measured on day 5 by means of MTT-assay and compared to MCF-7 cells transfected with a control vector.

Results: The proliferation of MCF-7/PGRMC1-3HA cells was increased in the presence of E2 by about 150% as compared to control cells with a value of about 50%. In the 'E2-first' regimen Tam could not abrogate the E2-induced proliferation. In the 'Tam-first' and 'continuous' regimen the E2-induced proliferation was reduced by Tam. However Tam showed a concentration-dependent agonistic effect of about 40% at 10-6 M Tam. In control cells no such effect could be observed.

Conclusion: Overexpression of PGRMC1 sensitizes MCF-7 towards E2-induced proliferation. Preliminary data suggest a possible influence of PGRMC1 on the development of resistance towards tamoxifen probably mediated via cross-talk with ERα.