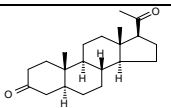
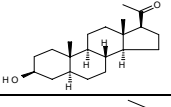
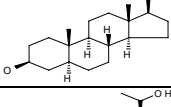
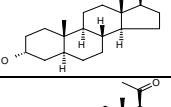
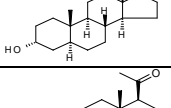
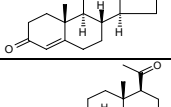
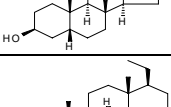
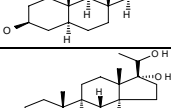
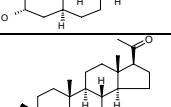
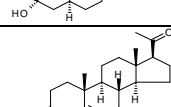
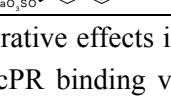


Table 2: Summary of the structure-activity-relationship (SAR) analysis of progestins to cPR.

| Progestins | Structure | PR binding GoldScore | Experimental Value | BrdU Incorporation |
|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------|--------------------|--------------------|
| 5 α -Dihydroprogesterone (5 α -Pregnane-3, 20-dione) |  | 65.31 | 96.8127 nM | -- |
| Epiallopregnanolone (3 α -hydroxy-5 β -pregnan-20-one) |  | 63.86 | 594.922 nM | + |
| 5 α -Pregnan-3 β -ol |  | 62.93 | No binding | -- |
| Allopregnanediol (5 α -pregn-an-3 α , 20 α -diol) |  | 62.69 | No Binding | -- |
| Allopregnanolone (3 α -hydroxy-5 α -pregnan-20-one, AP α) |  | 62.08 | No Binding | +++ |
| Progesterone (pregn-4-ene-3, 20-dione) |  | 61.11 | 9.00593 nM | +++ |
| Epipregnanolone (3 β -hydroxy-5 β -pregnan-20-one, AP β) |  | 60.56 | 28.359 nM | -- |
| 3 β -hydroxy-5 α -pregnan-20-one |  | 58.77 | No Binding | -- |
| Allopregnanetriol (5 α -pregnan-3 α , 17, 20 α -triol) |  | 57.86 | No Binding | + |
| Ganaxolone (3 α -hydroxy-5 β -methyl-5 α -pregnan-20-one) |  | 50.35 | No Binding | ++ |
| Pregnanolone Sulfate (5-pregnan-3 β -ol-20-one-3-sulfate) |  | 29.28 | No Binding | -- |

All steroids tested for proliferative effects in rNPCs were listed with their chemical structure (2nd column) and predicted cPR binding value from computational modeling (3rd column). GoldScore, which has been optimized for the prediction of ligand binding positions, was listed in the 3rd column. A higher GoldScore indicates a higher binding affinity to cPR based on the modeling. The PR binding affinity and selectivity of the steroids were confirmed determined by a cPR fluorescent polarization competitive binding assay and polarization values were plotted against the logarithm of the test compound concentration. IC₅₀ value, the concentration of the test compound that displaces half of the PL Red from PR, was determined (4th column). PR and PL Red (equivalent to 0% inhibition) was used as negative control and free PL Red (equivalent to 100% inhibition) was used as positive control. Proliferative effects from BrdU chemiluminescence ELISA were summarized in the last column. +: pro-proliferative effect. -: no effect on proliferation.