

# QSAR model for Estrogen Receptor Alpha (ER $\alpha$ ) antagonism (v1.0)

## ProtoED

ProtoED is a computational (*in silico*) tool focused on the prediction of endpoints related with the toxicity of chemical substances. It includes a variety of *in vitro* and *in vivo* tests in humans, animals, microorganisms and cell lines.

ProtoED mainly includes, but is not limited to, endpoints used by REACH, a European Union regulation, adopted to improve the protection of human health and the environment from the risks that can be posed by chemicals, while enhancing the competitiveness of the EU chemicals industry.

## Endpoint

### Human health effects: Estrogen receptor alpha antagonism

Estrogen receptor alpha (ER $\alpha$ ) is a member of the nuclear receptor superfamily of transcription factors whose activity is primarily regulated by binding of estrogen/estradiol (E2). E2 plays an indispensable role in growth, development, reproduction, and maintenance of numerous physiological systems in mammals. Estrogen receptor alpha antagonism occurs when substances bind to ER $\alpha$  but do not activate it. Instead, they competitively inhibit the binding of endogenous estrogens, thus blocking the receptor-mediated transcriptional response. This mechanism can disrupt normal estrogenic signaling pathways and may have therapeutic or endocrine-disruptive implications.

## Metrics

### Training set

| Experimental values | QSAR predictions |            |
|---------------------|------------------|------------|
|                     | inactive         | antagonist |
| inactive            | 360              | 106        |
| antagonist          | 85               | 401        |

### Validation set


| Experimental values | QSAR predictions |            |
|---------------------|------------------|------------|
|                     | inactive         | antagonist |
| inactive            | 114              | 45         |
| antagonist          | 28               | 135        |

| Parameters                       | Training | Validation |
|----------------------------------|----------|------------|
| Accuracy                         | 0.80     | 0.77       |
| Sensitivity / recall             | 0.83     | 0.83       |
| Specificity                      | 0.77     | 0.72       |
| Precision                        | 0.79     | 0.75       |
| Negative predictive value        | 0.81     | 0.80       |
| F-score                          | 0.81     | 0.79       |
| Matthews Correlation Coefficient | 0.60     | 0.55       |
| Critical Success Index           | 0.68     | 0.65       |
| Area under the ROC               | 0.80     | 0.77       |

ProtoED is part of



ProtoPRED platform allows the easy, fast and user-friendly prediction of different properties of chemical compounds, using proprietary (Q)SAR models.

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