

Pharmacophore Synergism in Diverse Scaffolds Clinches Aurora Kinase B

Vijay H. Masand ^{1,*}, Sami A. Al-Hussain ², Mithilesh M. Rathore ¹, Sumer D. Thakur ³, Siddhartha Akasapu ⁴, Abdul Samad ⁵, Aamal A. Al-Mutairi ² and Magdi E. A. Zaki ^{2,*}

Statistical Parameters for Model-A:

$R^2_{tr} = 0.815$, $R^2_{adj.} = 0.812$, $R^2_{tr} - R^2_{adj.} = 0.003$, $LOF = 0.234$, $K_{xx} = 0.409$, $\Delta K = 0.045$, $RMSE_{tr} = 0.468$, $MAE_{tr} = 0.401$, $RSS_{tr} = 98.506$, $CCC_{tr} = 0.898$, $s = 0.473$, $F = 277.836$, $R^2_{cv} (Q^2_{loo}) = 0.808$, $R^2 - R^2_{cv} = 0.007$, $RMSE_{cv} = 0.477$, $MAE_{cv} = 0.408$, $PRESS_{cv} = 102.107$, $CCC_{cv} = 0.895$, $Q^2_{LMO} = 0.807$, $R^2_{Yscr} = 0.016$, $Q^2_{Yscr} = -0.02$, $RMSE_{ex} = 0.446$, $MAE_{ex} = 0.373$, $PRESS_{ext} = 22.264$, $R^2_{ex} = 0.814$, $Q^2 - F^1 = 0.811$, $Q^2 - F^2 = 0.811$, $Q^2 - F^3 = 0.833$, $CCC_{ex} = 0.9$, $R^2 - ExPy = 0.814$, $R'^2 = 0.79$, $k' = 0.991$, $1 - (R^2 / R'^2) = 0.029$, $r'^2_m = 0.689$, $R_{\sigma^2} = 0.812$, $k = 1.005$, $1 - (R^2 - ExPy / R_{\sigma^2}) = 0.002$, $r^2_m = 0.779$,

Table S1. A comparison of two tautomeric forms YJA-T1 and YJA-T2 with respect to interactions with the receptor.

Tautomer with descriptors value	H-bonds formed with distance (Å) with angle (Donor-Hydrogen-Acceptor) (cut-off: 5 Å)	List of amino acids and solvent molecules whose at least one atom is within 5 Å from tautomeric form
YJA-T1 fsp3Csp2N5B = 0 N_H_2B = 6 fsp2Osp2C5B = 3	LYS122 at 1.668 with 159.8°, GLN145 at 2.251 with 142.4°, ALA173 at 1.952 with 163.9°	ARG97 , LEU99, PHE104, VAL107, ALA120, LYS122, LEU124, LEU138, GLU141, ILE142, GLN145, LEU154, MET156, LEU168, LEU170, PHE172, ALA173, GLU177, LEU223, ALA233, ASP234 , HOH2016
YJA-T2 fsp3Csp2N5B = 1 N_H_2B = 7 fsp2Osp2C5B = 3	LYS122 at 2.361 with 157.8°, GLN145 at 2.323 with 115.7°, ALA173 at 1.946 with 174.4°, HOH2108 2.222 with 106.7°	LEU99, PHE104, VAL107, ALA120, LYS122, LEU124, LEU138, GLU141, ILE142, GLN145, LEU154, MET156, LEU168, LEU170, PHE172, ALA173, ARG175 , GLU177, LYS180 , LEU223, ALA233, HOH2060 , HOH2108

Statistical parameters used for validation of QSAR models:

$$R^2 = 1 - \frac{\sum(y_i - \hat{y}_i)^2}{\sum(y_i - \bar{y})^2}$$

where y_i are the observed values of the response, \bar{y} the corresponding average, \hat{y} are the calculated values

$$Q^2 = 1 - \frac{\sum(y_i - \hat{y}_i)^2}{\sum(y_i - \bar{y})^2}$$

where y_i are the observed values of the response, \bar{y} the corresponding average, \hat{y} are the values predicted for each object when it is not in the training set.

$$Q_{F1}^2 = 1 - \frac{\sum_{i=1}^{n_{EXT}} (y_i - \hat{y}_i)^2}{\sum_{i=1}^{n_{EXT}} (y_i - \bar{y}_{TR})^2}$$

where y_i are the observed values of the response, \bar{y} the corresponding average, \hat{y} are the calculated values

$$Q_{F2}^2 = 1 - \frac{\sum_{i=1}^{n_{EXT}} (y_i - \hat{y}_i)^2}{\sum_{i=1}^{n_{EXT}} (y_i - \bar{y}_{EXT})^2}$$

where y_i are the observed values of the response, \bar{y} the corresponding average, \hat{y} are the calculated values

$$Q_{F3}^2 = 1 - \frac{\left[\sum_{i=1}^{n_{EXT}} (y_i - \hat{y}_i)^2 \right] / n_{EXT}}{\left[\sum_{i=1}^{n_{TR}} (y_i - \bar{y}_{TR})^2 \right] / n_{TR}}$$

where y_i are the observed values of the response, \bar{y} the corresponding average, \hat{y} are the calculated values

$$CCC = \frac{2 \sum_{i=1}^{n_{EXT}} (y_i - \bar{y})(\hat{y}_i - \bar{\hat{y}})}{\sum_{i=1}^{n_{EXT}} (y_i - \bar{y})^2 + \sum_{i=1}^{n_{EXT}} (\hat{y}_i - \bar{\hat{y}})^2 + n_{EXT} (\bar{y} - \bar{\hat{y}})^2}$$

$$k = \frac{\sum_{i=1}^{n_{EXT}} y_i \hat{y}_i}{\sum_{i=1}^{n_{EXT}} \hat{y}_i^2}$$

$$k' = \frac{\sum_{i=1}^{n_{EXT}} y_i \hat{y}_i}{\sum_{i=1}^{n_{EXT}} y_i^2}$$

$$r_m^2 = r^2 \left(1 - \sqrt{r^2 - r_0^2} \right)$$

$$\overline{r_m^2} = \frac{(r_m^2 + r_m'^2)}{2}$$

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n_{EXT}} (y_i - \hat{y}_i)^2}{n_{EXT}}}$$

$$MAE = \frac{\sum_{i=1}^{n_{EXT}} |y_i - \hat{y}_i|}{n_{EXT}}$$

where y_i are the observed values of the response, \bar{y} the corresponding average, \hat{y} are the calculated values