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### ACCEPTED MANUSCRIPT

# Molecular modeling on HIF-2 $\alpha$ -ARNT dimer destabilization caused by R171A and/or V192D mutations in HIF-2 $\alpha$

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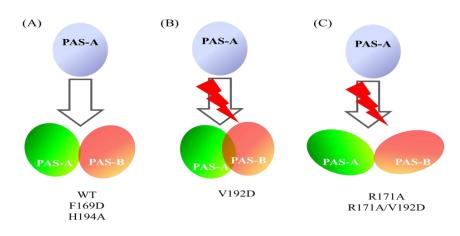
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#### **Graphical abstract**

(A) F169D and H194A barely alter the structure, and therefore act as WT proteins.(B) V192D brings PAS-A and PAS-B domains closer and shrinks the opening to

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