

Supplemental Information

Regulation of kinase activity in the *C. elegans* EGF receptor, LET-23

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Table S1, related to **Figure 1**. Primary sequence of EGF receptor kinase domains from different species used for generating a sequence alignment and phylogeny tree (Figure 1). The sequences were the same as used by Barberan and colleagues (Barberan et al., 2016), with the exception of those that contained significant truncations within the kinase domain regions.

Table S2, related to **Figure 1**. Sequence conservation within the receiver/activator interfaces and other motifs involved in allosteric activation of the human EGFR kinase, across 71 EGFR sequences analyzed in Figure 1. Reference sequence motifs in human EGFR are identified by the numbering of the most N-terminal residue in each motif (numbering is of the mature EGFR, without the 24 amino acid-long signal peptide). The scores represent the degree of conservation (1 – conserved, 0.5 – partially conserved, 0 – not conserved) determined by comparing each sequence to human EGFR. Activator and receiver interfaces were determined to be conserved when there was no (score 1) or only one substitution in the interface that significantly altered chemical properties, such as substitution of a hydrophobic residue with a charged residue (score 0.5). In all other instances, we considered these interfaces as not conserved (score 0). The juxtamembrane (JM) latch sequence was scored based on overall similarity to the human EGFR sequence, with score 1 being most similar, score 0.5 being somewhat similar and score 0 being significantly divergent from the human sequence. When activation loop tyrosine was present in the same position within the activation loop as it is located in the activation loop in human EGFR, it was scored as “YES”. Presence of the activation loop tyrosine C-terminally or N-terminally to the position in the human EGFR sequence was marked by “C-term” or “N-term”, respectively. In cases where more than one tyrosine residue was found in the activation loop, the number of tyrosines is indicated in parentheses. The receptor was marked as a pseudokinase (denoted as “Pseudo”) when one or more motifs important for kinase catalysis were found mutated. In all categories, sequences that were considered conserved are colored in green.

Figure S1, related to **Figure 2**.

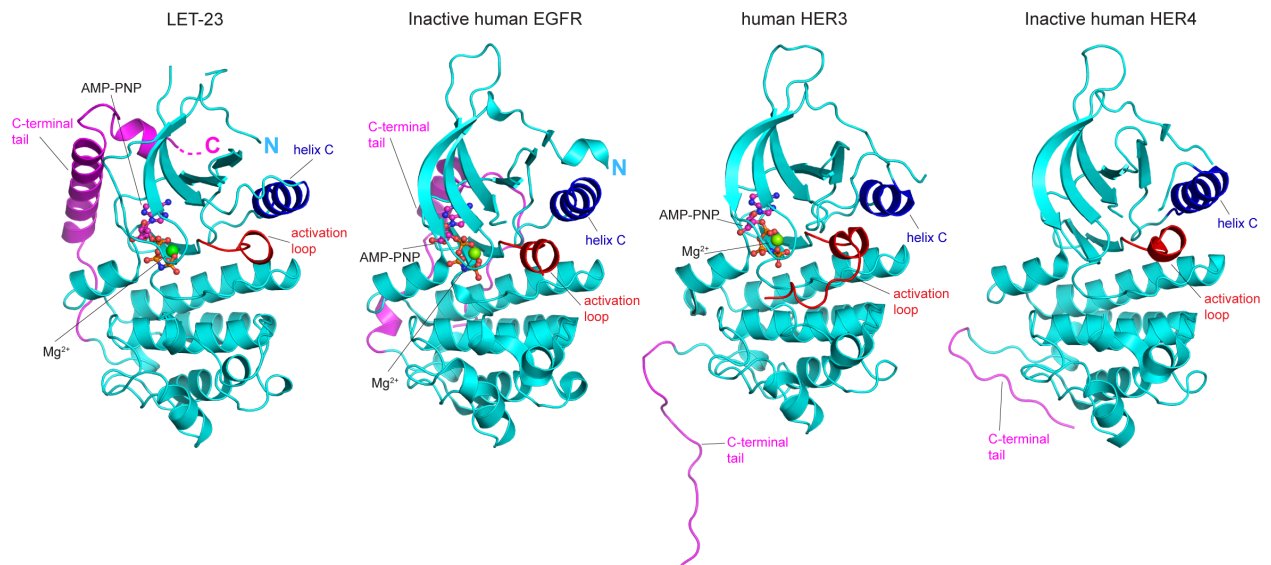


Figure S1, related to **Figure 2**. Comparison between the inactive kinase domain structures of the human EGFR family members, including EGFR (PDB ID: 5CNO), HER3 (PDB ID: 3KEX) and HER4 (PDB ID: 3BBW), to the structure of the inactive LET-23 kinase domain.