Analysis of regulatory mechanism after ErbB4 gene mutation based on local modeling methodology

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ABSTRACT. ErbB4 is an oncogene belonging to the epidermal growth factor receptor family and contributes to the occurrence and development of multiple cancers, such as gastric, breast, and colorectal cancers. Therefore, studies of the regulation of ErbB4 in cancerigenic pathway will advance molecular targeted therapy. Advanced bioinformatic analysis softwares, such as ExPASy, Predictprotei, QUARK, and I-TASSER, were used to analyze the regulatory mechanism after ErbB4 gene mutation in terms of amino acid sequence, primary, secondary, and tertiary structure of the protein and upstream-downstream receptor/ligands. Mutation of the 19th and 113th amino acids at the carboxyl terminus of ErbB4 protein did not affect its biological nature, but its secondary structure changed and protein binding sites were near 2 mutational sites; moreover, after mutation introduction, additional binding sites were observed. Tertiary structure modeling indicated that local structure of ErbB4 was changed from an α helical conformation into a β chain folding structure; the α helical conformation is the

functional site of protein, while active sites are typically near junctions between helical regions, thus the helical structures are easily destroyed and change into folding structures or other structures after stretching. Mutable sites of ErbB4 is exact binding sites where dimer formed with other epidermal growth factor family proteins; mutation enabled the ErbB4 receptor to bind to neuregulin 1 ligand without dimer formation, disrupting the signal transduction pathway and affecting ErbB4 function.

Key words: ErbB4; Gene mutation; Molecular modeling

