**Table 3** Frequently observed mutated GPCRs in cancer. This list is adapted from the review: “An Insight into GPCR and G-Proteins as Cancer Drivers” by Kim et al.(Chaudhary & Kim, 2021).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Receptor** | **Class** | **Location of mutations** | **Effect of mutated receptor** | **Ref** |
| Thyroid-stimulating hormone  receptor (TSHR) | Class A | N-terminal, ICL3, TM6, ECL2, ECL3 | ↑cAMP | (Bonomi *et al.*, 2001; Miyai, 2007) |
| Melanocortin 1 receptor  (MC1R) | Class A | TM2, ICL2 | activation of MAPK/ERK, mTor | (JA & Bishop, 2005; Turan *et al.*, 2012) |
| Melanocortin 2 receptor  (MC2R) | Class A | S74I,R137W, Y254C | defective trafficking to cell surface | (Flück *et al.*, 2002) |
| Lutropin receptor  (LHR) | Class A | TM3, TM6 | ↑cAMP | (G. Liu *et al.*, 1999) |
| Smoothened receptor  (SMO) | Class F | N-terminal, TM6, TM7 | CA of Hedgehog pathway | (Reifenberger *et al.*, 1998; Wang *et al.*, 2014) |
| Follicle-stimulating hormone receptor (FSHR) | Class A | ECL2, TM4, TM6 | ↑cAMP | (Tao, 2008) |
| Glutamate family of G protein-linked receptors (GRM1–8) | Class A | N-terminal, ECL1, ECL2, C-terminal | activation of the Hedgehog pathway | (Elia *et al.*, 2012; Kan *et al.*, 2010) |
| Muscarinic acetylcholine receptor (mAChR) | Class A | N-terminal, TM2, TM3, ICL3 | activating and inactivating mutations | (Kruse *et al.*, 2012) |
| Lysophosphatidic acid receptor (LPAR) | Class A | ICL2, ICL4, TM4, TM6, TM7 | activating mutations | (Raza *et al.*, 2014) |
| Sphingosine 1-phosphate receptor (S1PR) | Class A | N-terminal, TM4 | inactivating mutations | (Obinata *et al.*, 2014) |
| Abbreviations: ICL- Intracellular loop, ECL- Extracellular loop, TM- Transmembrane α-helix, CA- constitutive activity | | | | |