Pharmacophore-driven Identification of Human Glutaminyl Cyclase Inhibitors from Foods, Plants and Herbs Unveil the Bioactive Property and Potential of Azaleatin for the Treatment of Alzheimer’s Disease

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Figure S1. The results of ligand-pharmacophore (Phar-MERGE) mapping of TOP 11 hits screened from Natural Product database. The top 11 candidates identified from IBS database are mapped with pharmacophore model, Phar-MERGE. The fitting values and the compound named by IBS database are shown. (Pharmacophore features are color-coded as follows: cyan, hydrophobic; green, hydrogen-bond acceptor; orange, ring aromatic; purple, zinc ion binder and dark gray, excluded volume.)
Figure S2. The results of ligand-pharmacophore (Phar-SEN) mapping of hits screened from Traditional Chinese Medicine database. The chemical structures of identified 18 candidates (TCM7–TCM24) mapped with Phar-SEN. (Pharmacophore features are color-coded as follows: cyan, hydrophobic; green, hydrogen-bond acceptor; orange, ring aromatic; purple, zinc ion binder and dark gray, excluded volume.)
Figure S3. The detailed chemical structures of hits screened by Phar-MERGE from IBS database.
Figure S4. The detailed chemical structures of hits screened by Phar-SEN from TCM database. The 2D chemical structures and inhibition % (at 100 μM) of TCM7~TCM24 against hQC are shown.
Figure S5. The molecular dynamics simulations of hQC-TCM1. The trajectory profiles of total energy and kinetic energy of hQC in complex with TCM1 during MD simulation time for 2,000 ps are presented.
Figure S6. The molecular dynamics simulations of hQC-TCM2 complex. The total energy and kinetic energy as a function of simulation time for 2,000 ps are shown.
Figure S7. The molecular dynamics simulations of hQC-TCM3. The trajectory profiles of total energy and kinetic energy of hQC in complex with TCM3 during MD simulation time for 2,000 ps are presented.
Figure S8. The molecular dynamics simulations of hQC-TCM4 complex. The total energy and kinetic energy as a function of simulation time for 2,000 ps are shown.
Figure S9. The molecular dynamics simulations of hQC-TCM5. The trajectory profiles of total energy and kinetic energy of hQC in complex with TCM5 during MD simulation time for 2,000 ps are presented.
Figure S10. The molecular dynamics simulations of hQC-TCM6 complex. The total energy and kinetic energy as a function of simulation time for 2,000 ps are shown.
Figure S11. The detailed molecular interactions of IBS11 targeting hQC. The detailed molecular interactions of IBS11 binding to hQC was analyzed and shown. In the left panel, IBS11 is presented as stick (deep-blue); hQC is shown as ribbon (gray); zinc ion is displayed as spheres (orange). In the right panel, IBS11 is colored in deep-blue and the active site residues of hQC are labeled. The dash lines colored in magenta, orange, black, cyan, and purple denote the hydrophobic interaction, anion-pi interaction, and coordination with zinc ion, pi-donor hydrogen bond, and pi-sigma interaction, respectively.