iScience, Volume *26*

Supplemental information

Structure-affinity and structure-residence time relationships of macrocyclic $G\alpha_q$ protein inhibitors

Jan H. Voss, Max Crüsemann, Christian R.O. Bartling, Stefan Kehraus, Asuka Inoue, Gabriele M. König, Kristian Strømgaard, and Christa E. Müller

Supporting Information

Structure-affinity and structure-residence time relationships of macrocyclic $G\alpha_q$ protein inhibitors

Jan H. Voss[1], Max Crüsemann[2], Christian R. O. Bartling[3], Stefan Kehraus[2], Asuka Inoue[4], Gabriele M. König[2], Kristian Strømgaard[3] and Christa E. Müller[1]

[1] PharmaCenter Bonn, Pharmaceutical Institute, Pharmaceutical & Medicinal Chemistry, University of Bonn, An der Immenburg 4, D-53121 Bonn

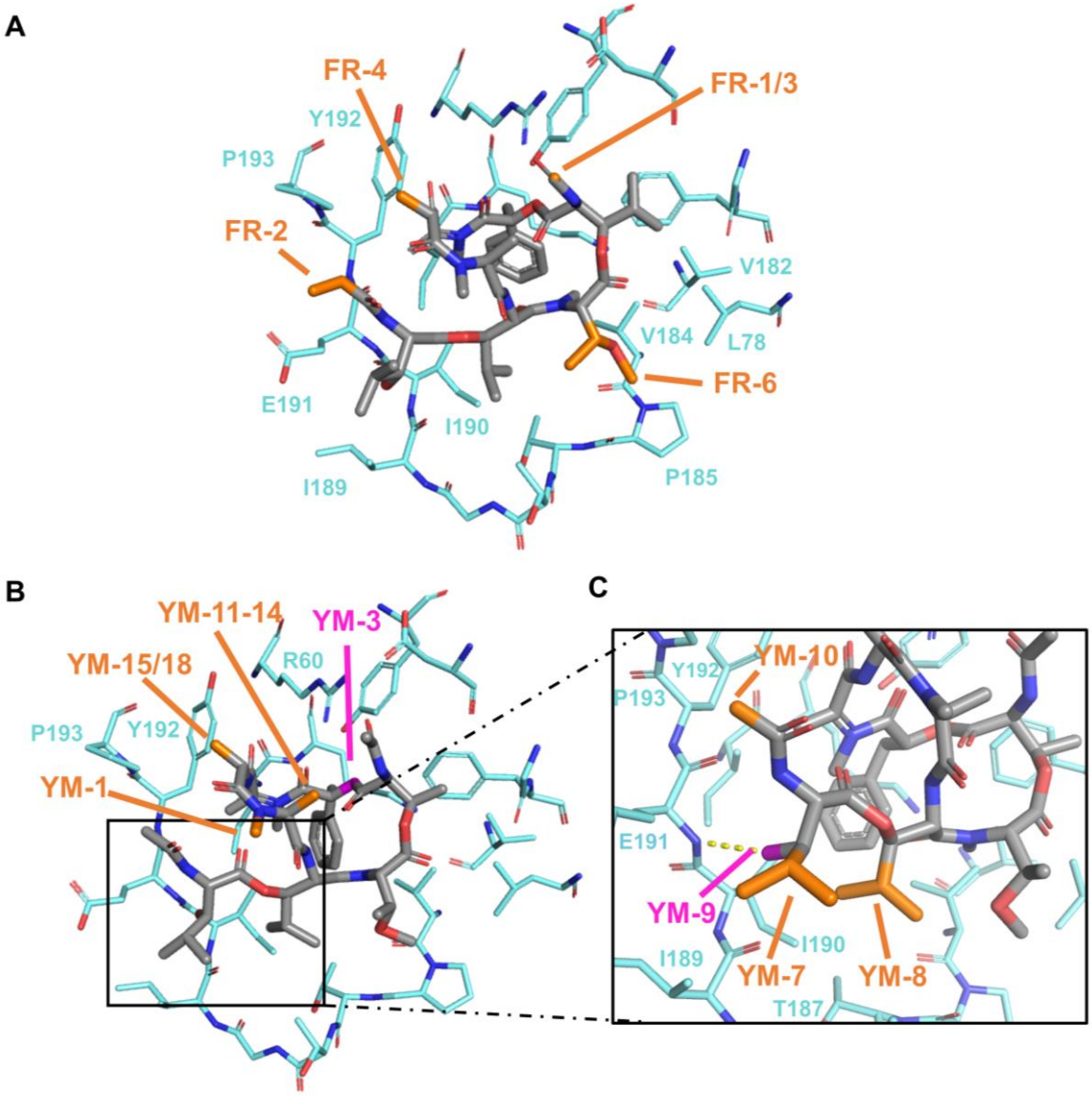
[2] Institute of Pharmaceutical Biology, University of Bonn, Nussallee 6, 53115 Bonn, Germany

[3] Department of Drug Design and Pharmacology, Center for Biopharmaceuticals, University of Copenhagen, Universitetsparken 2, 2100 Copenhagen, Denmark

[4] Tohoku University, Graduate School of Pharmaceutical Sciences, Sendai, Miyagi 980-8578 Japan

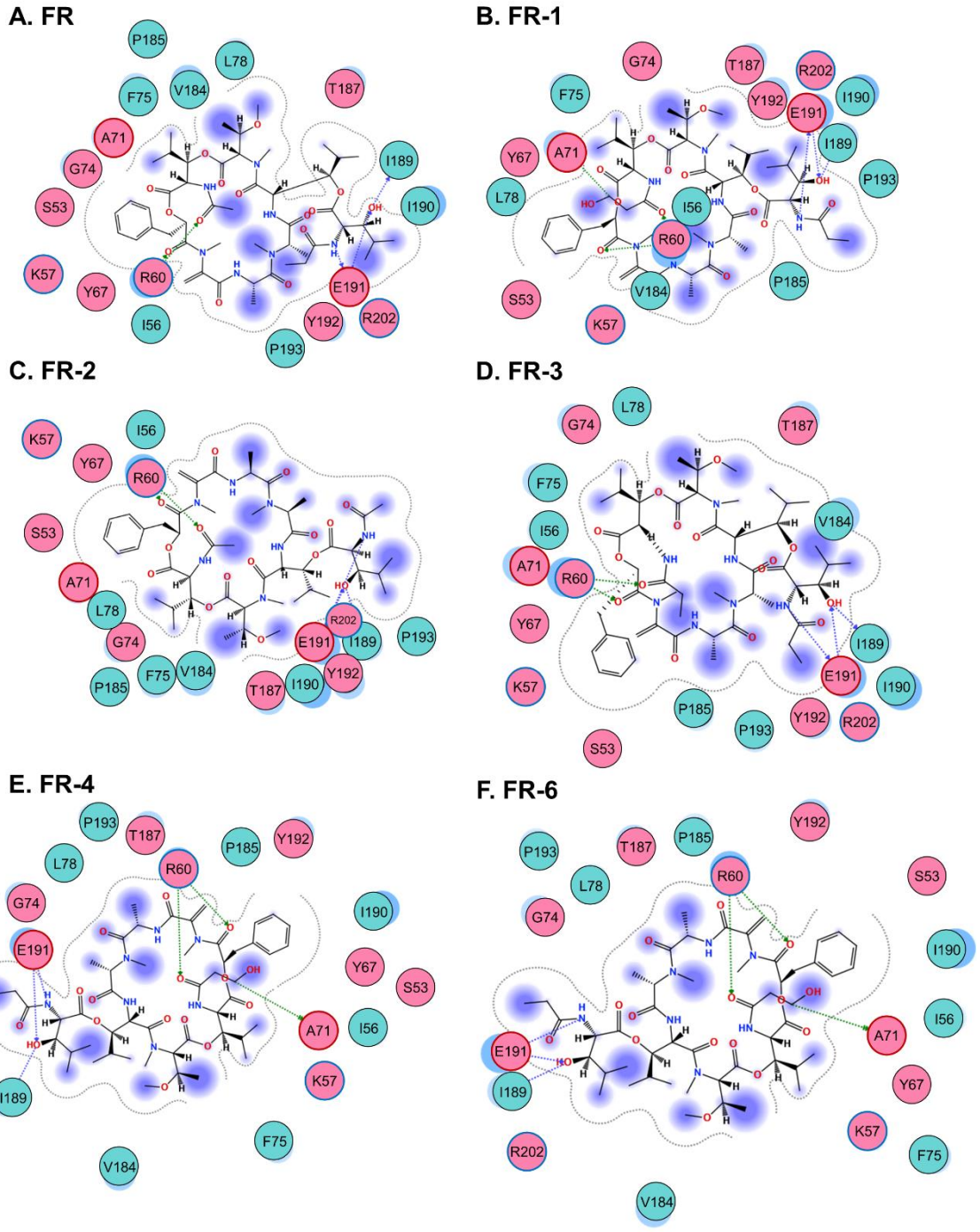
Table of Contents

Supporting Figure S1. Three-dimensional visualization of the binding poses of FR and YM and their derivatives, related to Fig. 6.



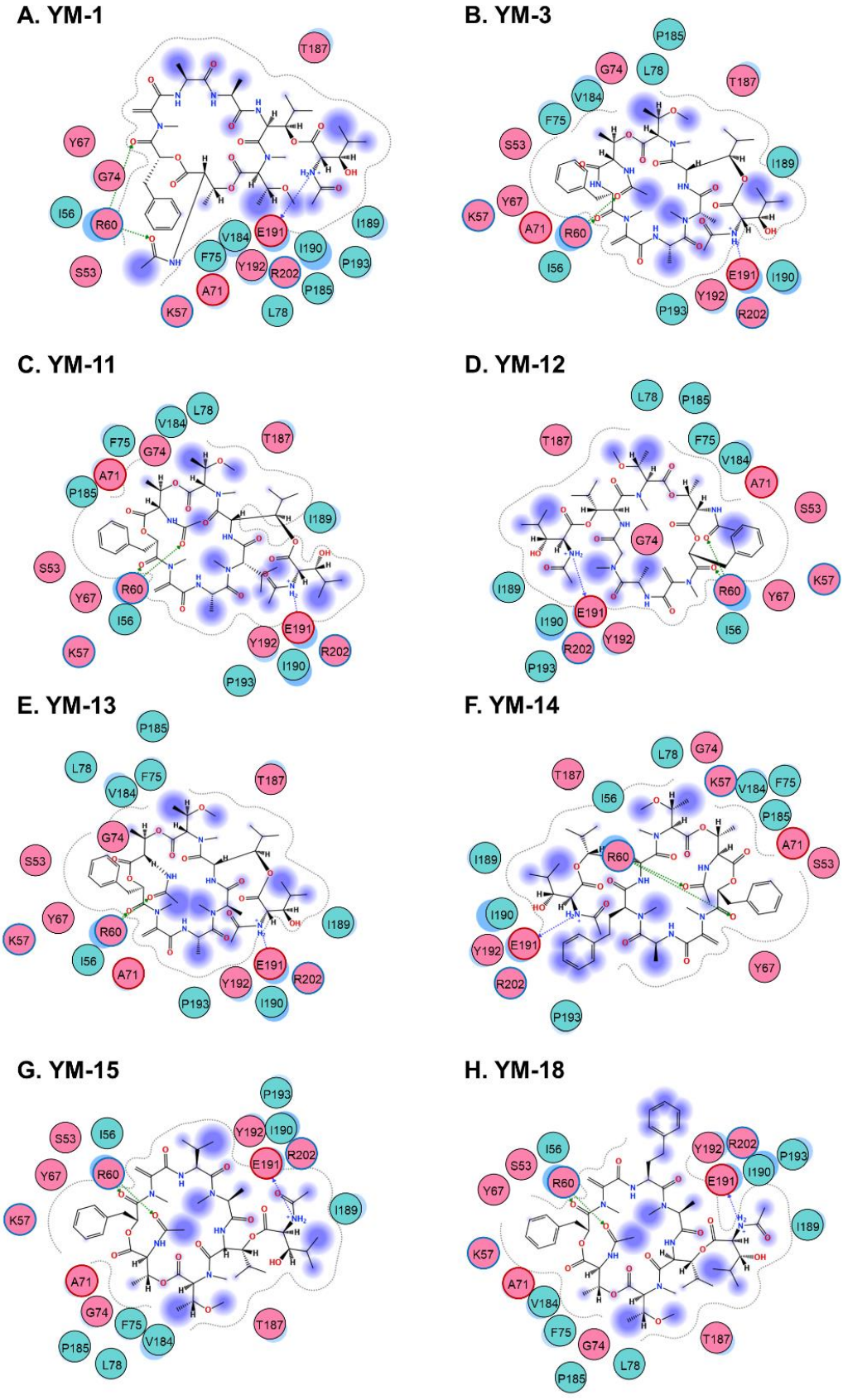
Three-dimensional visualization of the binding poses of FR and its derivatives (A) and YM and its derivatives (B, C), related to Fig. 6. The $G\alpha_q$ binding site is shown as cyan sticks, the inhibitors are shown in gray, and modifications of the inhibitors are highlighted in orange or purple. The inhibitors were modeled based on docked pose of FR (A) and the crystal structure pose of YM (B, C), respectively.

Supporting Figure S2. 2D-interaction maps of FR and its derivatives, related to Fig. 6.



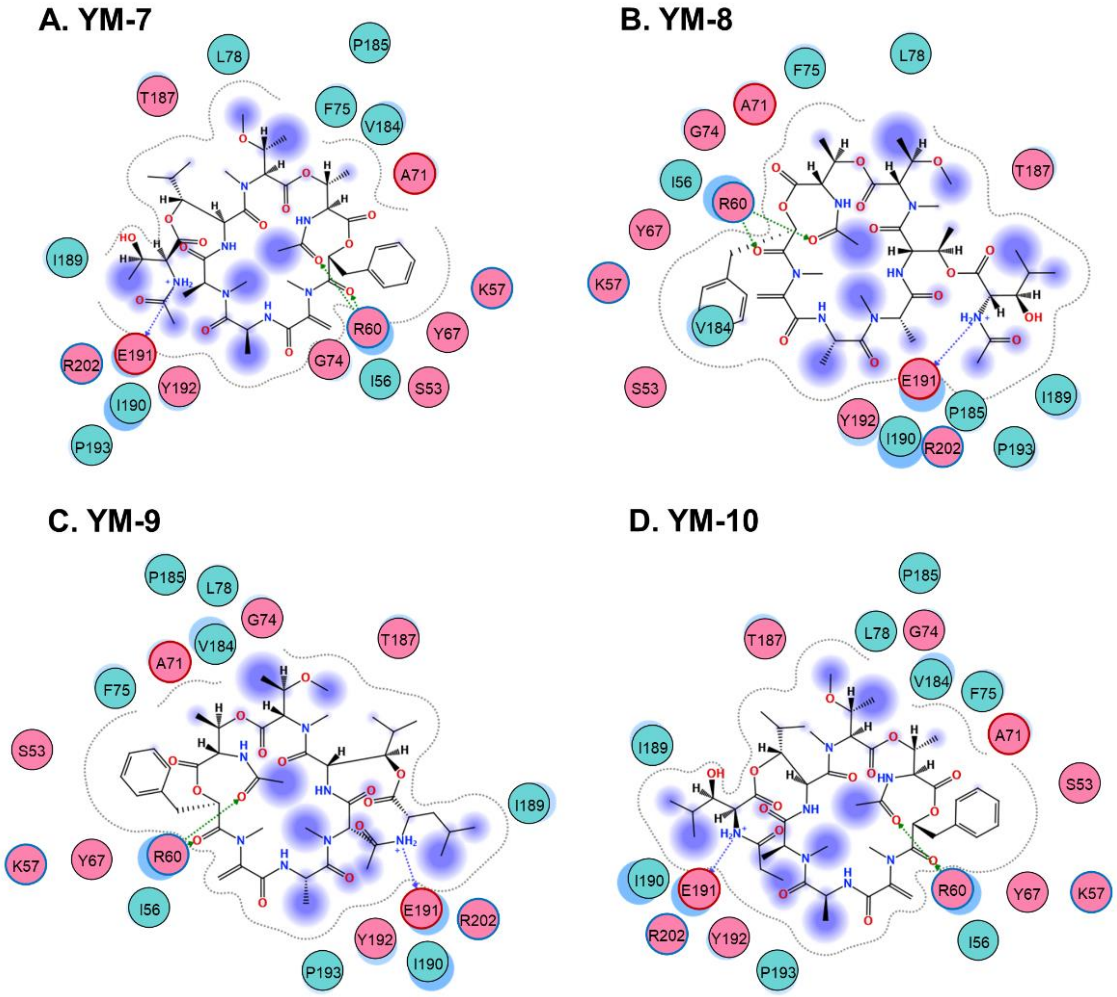
Predicted 2D-interaction maps of FR and its derivatives within the binding pocket of the $G\alpha_q$ protein, related to Fig. 6. Interactions were modeled based on the docked pose of FR. Maps were generated by MOE (Chemical Computing Group, Cambridge), polar residues are shown in red (acidic and basic residues with red and blue outlines, respectively), hydrophobic residues are displayed in green, blue shades at the residues indicate ligand contacts, and blue highlights at the ligand indicate solvent exposure.

Supporting Figure S3. 2D-interaction maps of the YM derivatives YM-1, -3, -11-15, and -18, related to Fig. 6.



Predicted 2D-interaction maps of the YM derivatives YM-1, -3, -11-15, and -18 within the binding pocket of the $G\alpha_q$ protein, related to Fig. 6. Interactions were modeled based on the crystal structure pose of YM. Maps were generated by MOE (Chemical Computing Group, Cambridge), polar residues are shown in red (acidic and basic residues with red and blue outlines, respectively), hydrophobic residues are displayed in green, blue shades at the residues indicate ligand contacts, and blue highlights at the ligand indicate solvent exposure.

Supporting Figure S4. 2D-interaction maps of the YM derivatives YM-7-10, related to Fig. 6.



Predicted 2D-interaction maps of the YM derivatives YM-7-10 within the binding pocket of the $G\alpha_q$ protein, related to Fig. 6. Interactions were modeled based on the crystal structure pose of YM. Maps were generated by MOE (Chemical Computing Group, Cambridge), polar residues are shown in red (acidic and basic residues with red and blue outlines, respectively), hydrophobic residues are displayed in green, blue shades at the residues indicate ligand contacts, and blue highlights at the ligand indicate solvent exposure.