



Project 1 - König/Crüsemann lab


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	<p>Biosynthesis of the selective Gq protein inhibitor FR900359 as basis for compound supply and structural modifications</p>
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Publications

Krome AK, Becker T, Kehraus S, Schiefer A, Gütschow M, Chaverra-Muñoz L, Hüttel S, Jansen R, Stadler M, Ehrens A, Pogorevc D, Müller R, Hübner MP, Hesterkamp T, Pfarr K, Hoerauf A, Wagner KG, König GM. Corallopyronin A: antimicrobial discovery to preclinical development. *Nat Prod Rep*. 2022 Jun 22. doi: 10.1039/d2np00012a. Epub ahead of print. PMID: 35730490. 

Wirtz DA, Ludwig KC, Arts M, Marx CE, Krannich S, Barac P, Kehraus S, Josten M, Henrichfreise B, Müller A, König GM, Peoples AJ, Nitti A, Spoering AL, Ling LL, Lewis K, Crüsemann M, Schneider T. (2021) *Biosynthesis and Mechanism of Action of the Cell Wall Targeting Antibiotic Hypeptin*. **Angew Chem Int Ed Engl**. 60(24):13579-13586. doi: 10.1002/anie.202102224. Epub 2021 May 7. PMID: 33768646; PMCID: PMC8252469. 

Klöppel S, Richarz R, Wirtz DA, Vasenda N, König GM, Crüsemann M. (2021) *A Specialized Dehydrogenase Provides l-Phenyllactate for FR900359 Biosynthesis*. **Chembiochem**. doi: 10.1002/cbic.202100569. Epub ahead of print. PMID: 34846772. 

Hanke W, Patt J, Alenfelder J, Voss JH, Zdouc MM, Kehraus S, Kim JB, Grujičić GV, Namasivayam V, Reher R, Müller CE, Kostenis E, Crüsemann M, König GM. (2021) *Feature-Based Molecular Networking for the Targeted Identification of G_q-Inhibiting FR900359 Derivatives*. **J Nat Prod**. doi: 10.1021/acs.jnatprod.1c00194. Epub 2021 Jul 1. PMID: 34197116. 

Hermes C, König GM, Crüsemann M. (2021) *The chromodepsins - chemistry, biology and biosynthesis of a selective G_q inhibitor natural product family*. **Nat Prod Rep**. doi: 10.1039/d1np00005e. Epub ahead of print. PMID: 33998635. 

Schlegel JG, Tahoun M, Seidinger A, Voss JH, Kuschak M, Kehraus S, Schneider M, Matthey M, Fleischmann BK, König GM, Wenzel D, Müller CE. (2021) *Macrocyclic G_q Protein Inhibitors FR900359 and/or YM-254890-Fit for Translation?* **ACS Pharmacol Transl Sci**. doi: 10.1021/acspsci.1c00021. PMID: 33860209; PMCID: PMC8033771.



Patt J, Alenfelder J, Pfeil EM, Voss JH, Merten N, Eryilmaz F, Heycke N, Rick U, Inoue A, Kehraus S, Deupi X, Müller CE, König GM, Crüsemann M, Kostenis E. (2021) *An experimental strategy to probe Gq contribution to signal transduction in living cells*. **J Biol Chem**.

doi: <https://doi.org/10.1016/j.jbc.2021.100472>

Hermes C, Richarz R, Wirtz DA, Patt J, Hanke W, Kehraus S, Voß JH, Küppers J, Ohbayashi T, Namasivayam V, Alenfelder J, Inoue A, Mergaert P, Gütschow M, Müller CE, Kostenis E, König GM, Crüsemann M. (2021) *Thioesterase-mediated side chain transesterification generates potent Gq signaling inhibitor FR900359*.

Nat Commun. doi: [10.1038/s41467-020-20418-3](https://doi.org/10.1038/s41467-020-20418-3).

Kuschak M, Schlegel JG, Schneider M, Kehraus S, Voss JH, Seidinger A, Matthey M, Wenzel D, Fleischmann BK, König GM, Müller CE. (2020) *Sensitive LC-MS/MS Method for the Quantification of Macrocyclic Gαq Protein Inhibitors in Biological Samples*. **Front Chem**. doi: [10.3389/fchem.2020.00833](https://doi.org/10.3389/fchem.2020.00833). PMID: 33173765; PMCID: PMC7540253.

Kuschak M, Namasivayam V, Rafehi M, Voss JH, Garg J, Schlegel JG, Abdelrahman A, Kehraus S, Reher R, Küppers J, Sylvester K, Hinz S, Matthey M, Wenzel D, Fleischmann BK, Pfeifer A, Inoue A, Gütschow M, König GM, Müller CE. (2020) *Cell-permeable high-affinity tracers for G_q proteins provide structural insights, reveal distinct binding kinetics and identify small molecule inhibitors*. **Br J Pharmacol**. doi: [10.1111/bph.14960](https://doi.org/10.1111/bph.14960). Epub 2020 Feb 11. PMID: 31881095; PMCID: PMC7070167.

Malfacini D, Patt J, Annala S, Harpsøe K, Eryilmaz F, Reher R, Crüsemann M, Hanke W, Zhang H, Tietze D, Gloriam DE, Bräuner-Osborne H, Strømgaard K, König GM, Inoue A, Gomez J, Kostenis E. (2019) *Rational design of a heterotrimeric G protein α subunit with artificial inhibitor sensitivity*. **J Biol Chem**. doi:

[10.1074/jbc.RA118.007250](https://doi.org/10.1074/jbc.RA118.007250)

Imhof D, Reher R, Kühl T, Annala S, Benkel T, Kaufmann D, Nubbemeyer B, Odhiambo JP, Heimer P, Bäuml CA, Kehraus S, Crüsemann M, Kostenis E, Tietze D, König GM. (2018) *Deciphering specificity determinants for FR900359-derived Gαq inhibitors based on computational and structure-activity studies*. **ChemMedChem** doi:

[10.1002/cmdc.201800304](https://doi.org/10.1002/cmdc.201800304)

Grundmann M, Merten N, Malfacini D, Inoue A, Preis P, Simon K, Rüttiger N, Ziegler N, Benkel T, Schmitt NK, Ishida S, Müller I, Reher

R, Kawakami K, Inoue A, Rick U, Kühl T, Imhof D, Aoki J, König GM, Hoffmann C, Gomeza J, Wess J, Kostenis E (2018); *Lack of beta-arrestin signaling in the absence of active G proteins*, **Nat Commun**, doi:10.1038/s41467-017-02661-3



Reher R, Kuschak M, Heycke N, Annala S, Kehraus S, Dai HF, Müller CE, Kostenis E, König GM, Crüsemann M. (2018) *Applying Molecular Networking for the Detection of Natural Sources and Analogues of the Selective Gq Protein Inhibitor FR900359*. **J Nat Prod**. doi:

10.1021/acs.jnatprod.8b00222



Crüsemann M, Reher R, Schamari I, Brachmann AO, Ohbayashi T, Kuschak M, Malfacini D, Seidinger A, Pinto-Carbó M, Richarz R, Reuter T, Kehraus S, Hallab A, Attwood M, Schiöth HB, Mergaert P, Kikuchi Y, Schäberle TF, Kostenis E, Wenzel D, Müller CE, Piel J, Carlier A, Eberl L, Koenig GM (2017); *Heterologous expression, biosynthetic studies and ecological function of the selective Gq-signaling inhibitor FR900359*, **Angew. Chem. Int. Ed.**, doi: 10.1002/anie.201707996



Murat S, Bigot M, Chapron J, König GM, Kostenis E, Battaglia G, Nicoletti F, Bourinet E, Bockaert J, Marin P, Vandermoere F. (2018) 5-HT_{2A} receptor-dependent phosphorylation of mGlu₂ receptor at Serine 843 promotes mGlu₂receptor-operated G_{i/o} signaling. **Mol Psychiatry** doi: 10.1038/s41380-018-0069-6



Matthey M, Roberts R, Seidinger A, Simon A, Schröder R, Kuschak M, Annala S, König GM, Müller CE, Hall IP, Kostenis E, Fleischmann BK, Wenzel D (2017); *Targeted inhibition of Gq signaling induces airway relaxation in mouse models of asthma*, **Sci Transl Med.**, 2, 407, doi:10.1126/scitranslmed.aag2288



Klepac K, Kilic A, Gnad T, Brown LM, Herrmann B, Wildermann A, Balkow A, Glöde A, Simon K, Lidell ME, Betz MJ, Enerbäck S, Wess J, Freichel M, Blüher M, König G, Kostenis E, Insel PA and Pfeifer A (2016); *The Gq signalling pathway inhibits brown and beige adipose tissue*, **Nat commun**, 7, 10895, doi: 10.1038/ncomms10895



Schrage R, Schmitz AL, Gaffal E, Annala S, Kehraus S, Wenzel D, Büllesbach KM, Bals T, Inoue A, Shinjo Y, Galandrin S, Shridhar N, Hesse M, Grundmann M, Merten N, Charpentier TH, Martz M,

Butcher AJ, Slodczyk T, Armando S, Effer M, Namkung Y, Jenkins L, Horn V, Stößel A, Dargatz H, Tietze D, Imhof D, Galés C, Drewke C, Müller CE, Hölzel M, Milligan G, Tobin AB, Gomeza J, Dohlmann HG, Sondek J, Harden K, Bouvier M, Laporte SA, Aoki J, Fleischmann BK, Mohr K, König GM, Tüting T and Kostenis E (2015); *The experimental power of FR900359 to study Gq-regulated biological processes*, **Nat. Commun.**, 6, 10156, doi: 10.1038/ncomms10156

