

## Tethered agonist exposure in intact adhesion GPCRs through intrinsic structural flexibility of the GAIN domain

Steffen Altrichter<sup>1,\*</sup>, Gerti Beliu<sup>2,\*</sup>, Ramon Guixà-González<sup>3,6,\*</sup>, Mareike Hemberger<sup>1</sup>, Ina Brauer<sup>1</sup>, Nicole Scholz<sup>1</sup>, Alexander Kuhlemann<sup>2</sup>, Guillermo Pérez-Hernández<sup>3</sup>, Hossein Batebi<sup>3</sup>, Florian Seufert<sup>3</sup>, Peter Hildebrand<sup>3,4,5,#</sup>, Markus Sauer<sup>2,#</sup>, Tobias Langenhan<sup>1,#v</sup>

<sup>1</sup>Rudolf Schönheimer Institute of Biochemistry, Division of General Biochemistry, Medical Faculty, Leipzig University, Johannisallee 30, 04103 Leipzig, Germany <sup>2</sup>Department of Biotechnology and Biophysics, Biocenter, University of Würzburg, Am Hubland, 97074 Würzburg, Germany <sup>3</sup>Institute of Medical Physics and Biophysics, Charité Medical University Berlin, Berlin, Germany <sup>4</sup>Institute for Medical Physics and Biophysics, Medical Faculty, Leipzig University, Härtelstrasse 16-18, 04107 Leipzig, Germany <sup>5</sup>Berlin Institute of Health, 10178 Berlin, Germany <sup>6</sup>Current affiliation: Laboratory of Biomolecular Research, Paul Scherrer Institute (PSI), 5232 Villigen PSI, Switzerland; Condensed Matter Theory Group, Paul Scherrer Institute (PSI), 5232 Villigen PSI, Switzerland

\*Equal contribution

#Co-correspondence

### Url links to the MDsrv sessions:

#### **Link 1**

L1 dynamic: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1.ngl)

#### **Link 2**

G1 dynamic: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/G1.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/G1.ngl)

#### **Link 3**

E5 static: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5\\_crevice.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5_crevice.ngl)

#### **Link 4**

E5 dynamic: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5.ngl)

#### **Link 5**

E5 +3 static: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5+3.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5+3.ngl)

#### **Link 6**

E5 +6 static: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5+6.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E5+6.ngl)

#### **Link 7**

E2 dynamic: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E2.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/E2.ngl)

#### **Link 8**

L1 Phe+3Lys dynamic: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1Phe+3Lys.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1Phe+3Lys.ngl)

#### **Link 9**

L1 Leu+6Lys dynamic: [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1Leu+6Lys.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1Leu+6Lys.ngl)

#### **Link 10**

L1 dynamic (ribbon representation): [proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1Ribbon.ngl](http://proteinformatics.uni-leipzig.de/html/mdsrv.html?load=file://base/aGPCRs/L1Ribbon.ngl)