

Scientific Module
of the Graduate School of CRC 1423

GPCR downstream effectors, it's all about enzyme kinetics

Dr. Sandra Berndt
Leipzig University, Medical Faculty

The activation of G protein-coupled receptors (GPCRs) stimulates signaling pathways that control major cellular responses. The signaling occurs in a G protein mediated, GRK-mediated or arrestin mediated manner. Each of these direct effectors can activate multiple other signaling proteins. Most key players in all GPCR signaling cascades are enzymes.

This module will give an overview about different downstream signaling cascades of GPCRs and how their allosteric regulation takes place. We will apply fundamental enzyme kinetic mechanisms for typical arrestin downstream effectors like MAPKs or Src kinases. Furthermore, the course provides practical aspects, an overview of different assays to study these enzymes and determine kinetical parameters. This will be followed by a lecture about different methods to inhibit enzymes and we will discuss different pharmacological drugs targeting signaling cascades. Here, the best examples are chemotherapeutic compounds like Dasatinib inhibiting Src kinases or Ulixertinib inhibiting ERK. The module will end with a future perspective for GPCR downstream effectors in pharmacological research.

Who:

PhD students of the CRC
(there will be a waiting list
for external PhD students)

When:

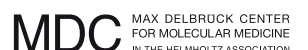
June 23-25, 2020

Where:

online via Zoom

Registration:

Please send an Email to:
juliane.adler@medizin.uni-leipzig.de





Program

PREPARATION

read two papers which will be given to you beforehand

WEDNESDAY

(06/23/21)
9:00-14:30

9:00-10:30

DOWNSTREAM EFFECTORS OF GPCRS

G protein mediated and arrestin-mediated signaling – a structural viewpoint
MAPK-cascade
Src kinases

10:30-11:00

DISCUSSION

11:10-12:10

FUNDAMENTAL MECHANISMS COMMON TO PROTEIN ACTION

Revision of enzyme kinetics
Michaelis – Menten equation
Reciprocal analysis
Practical considerations

12:10-12:40

DISCUSSION

13:30-14:30

DEMONSTRATION VIDEOS +EXTRA MATERIAL

THURSDAY

(06/24/21)
9:30-12:10

9:30-10:30

EXPERIMENTAL DESIGN

Practical aspects
Practice problems

10:30-11:00

DISCUSSION

13:30-14:30

DEMONSTRATION VIDEOS

FRIDAY

(06/25/21)
9:30-15:10

9:30-10:30

INHIBITION

reversible vs. suicide
competitive
Uncompetitive
mixed
Special cases
substrate and product inhibition
self-inhibition (already covered)
Examples for Src and MAP kinases as downstream effectors of GPCRS

10:30-11:00

DISCUSSION

11:10-12:10

DEMONSTRATION VIDEOS +EXTRA MATERIAL

13:10-15:10

PAPER-DISCUSSION

TAKE HOME - TEST

to get rewarded with 1 Credit Point

Morning-Sessions

Afternoon-Sessions