




# die Vorlage 2016

## Antibodies to $\beta$ adrenergic and muscarinic cholinergic receptors in patients with Chronic Fatigue Syndrome


[Madlen Loebel](#)<sup>a</sup>  , [Patricia Grabowski](#)<sup>a</sup>, [Harald Heidecke](#)<sup>b</sup>, [Sandra Bauer](#)<sup>a</sup>,  
[Leif G. Hanitsch](#)<sup>a</sup>, [Kirsten Wittke](#)<sup>a</sup>, [Christian Meisel](#)<sup>a c</sup>, [Petra Reinke](#)<sup>d e</sup>, [Hans-Dieter Volk](#)<sup>a e</sup>,  
[Øystein Fluge](#)<sup>f</sup>, [Olav Mella](#)<sup>f g</sup>, [Carmen Scheibenbogen](#)<sup>a e</sup>


Show more 

+ Add to Mendeley  Share  Cite

<https://doi.org/10.1016/j.bbi.2015.09.013> 

[Get rights and content](#) 

Under a Creative Commons [license](#) 

 open access

### Highlights

- $\beta$  AdR and muscarinic AChR autoantibodies are elevated in a subset of patients with CFS.
- High autoantibodies correlate with elevated IgG<sub>1-3</sub>, TPO and ANA antibodies and T cell activation.
- In patients responding to rituximab high pretreatment autoantibodies declined after treatment.

# Der Torschuß 2021 Erlangen/Berlin

ELSEVIER

Journal of Translational Autoimmunity



[J Transl Autoimmun.](#) 2021; 4: 100100.

Published online 2021 Apr 16. doi: [10.1016/j.jtauto.2021.100100](https://doi.org/10.1016/j.jtauto.2021.100100)

PMCID: PMC8049853

PMID: [33880442](https://pubmed.ncbi.nlm.nih.gov/33880442/)

## Functional autoantibodies against G-protein coupled receptors in patients with persistent Long-COVID-19 symptoms

[Gerd Wallukat](#)<sup>a,b,\*</sup> [Bettina Hohberger](#)<sup>c</sup> [Katrin Wenzel](#)<sup>b</sup> [Julia Fürst](#)<sup>d</sup> [Sarah Schulze-Rothe](#)<sup>b</sup> [Anne Wallukat](#)<sup>b</sup>  
[Anne-Sophie Hönicke](#)<sup>b</sup> and [Johannes Müller](#)<sup>b</sup>

▶ [Author information](#) ▶ [Article notes](#) ▶ [Copyright and License information](#) ▶ [PMC Disclaimer](#)

Associated Data

# Vor Erlangen



# Nach Erlangen



# Das fehlende Stück im Puzzle



# **GPCR AUTO-AK**

**G**-Protein  
**C**oupled  
**R**eceptors

# GPCR System?

Ein System mit 800 verschiedenen Rezeptoren

reguliert unsere Belastungen und fördert die Regeneration

Es gibt physiologische GPCR Auto - Ak

Es sind sg. funktionelle Auto-Ak, sie fördern oder bremsen multiple Zellprozesse

# **GPCR Historie**

Wallukat 89

Scheibenbogen 2016

Hohberger 2022

Babel 2023

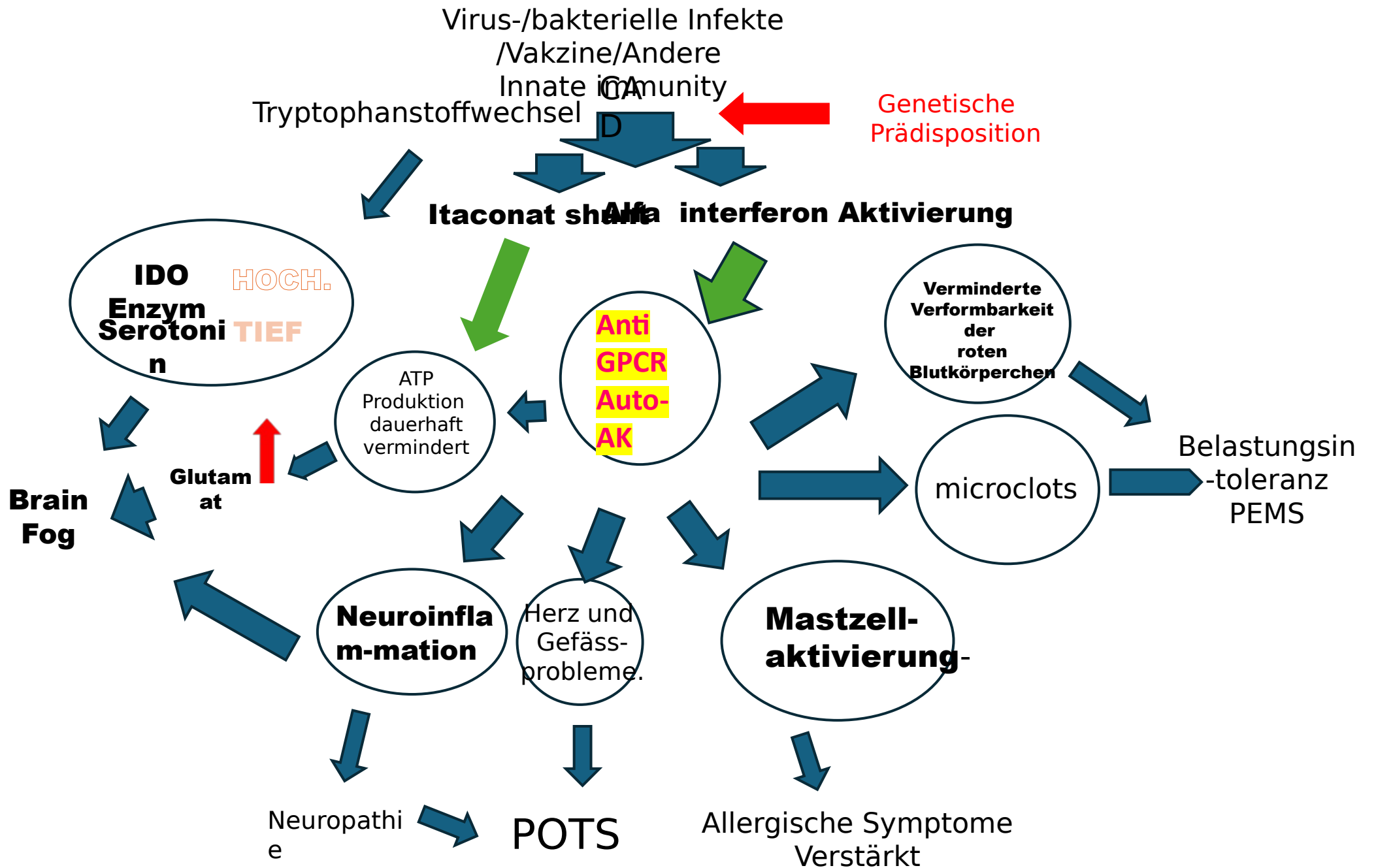
Metares 2023



**Diagnostik doch alles  
Klar!  
Therapie doch alles Klar!  
BC007  
Oder andere ?**

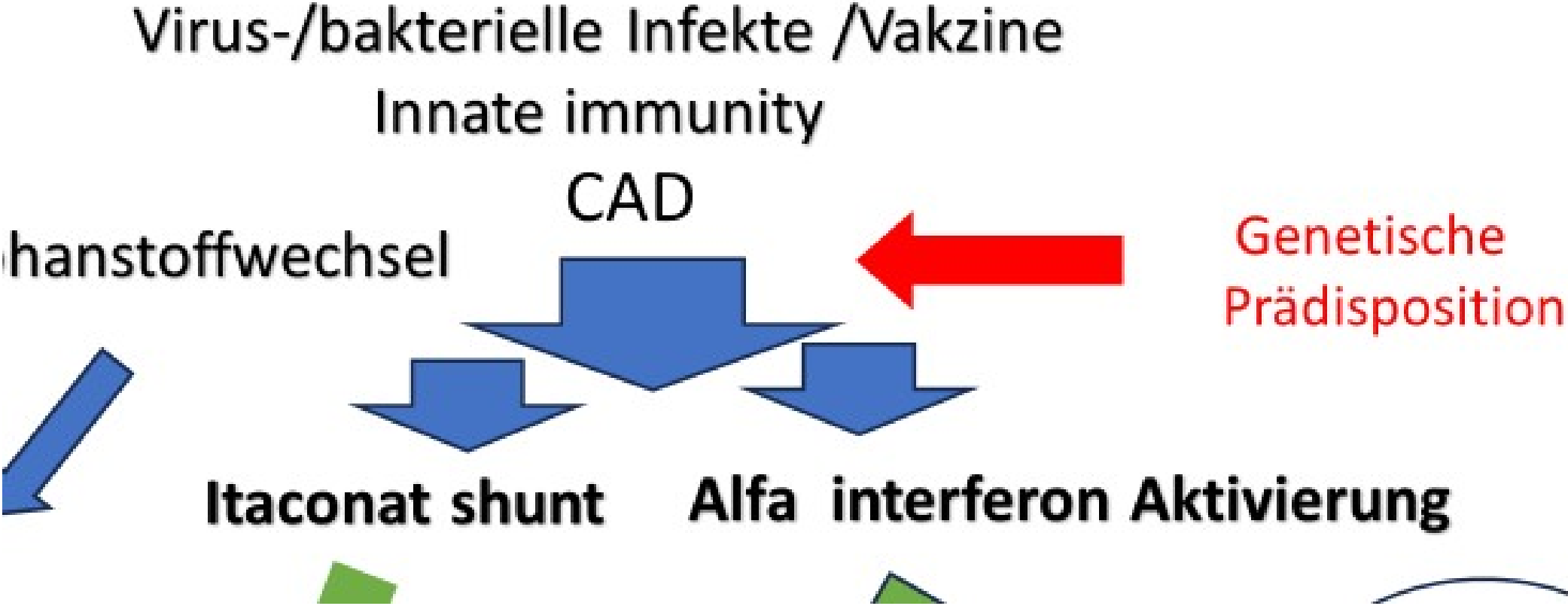
**aber warum passiert  
nichts !!!**

Dr.L.Habets  
Metares e.V Aachen  
Köln 20.1.24

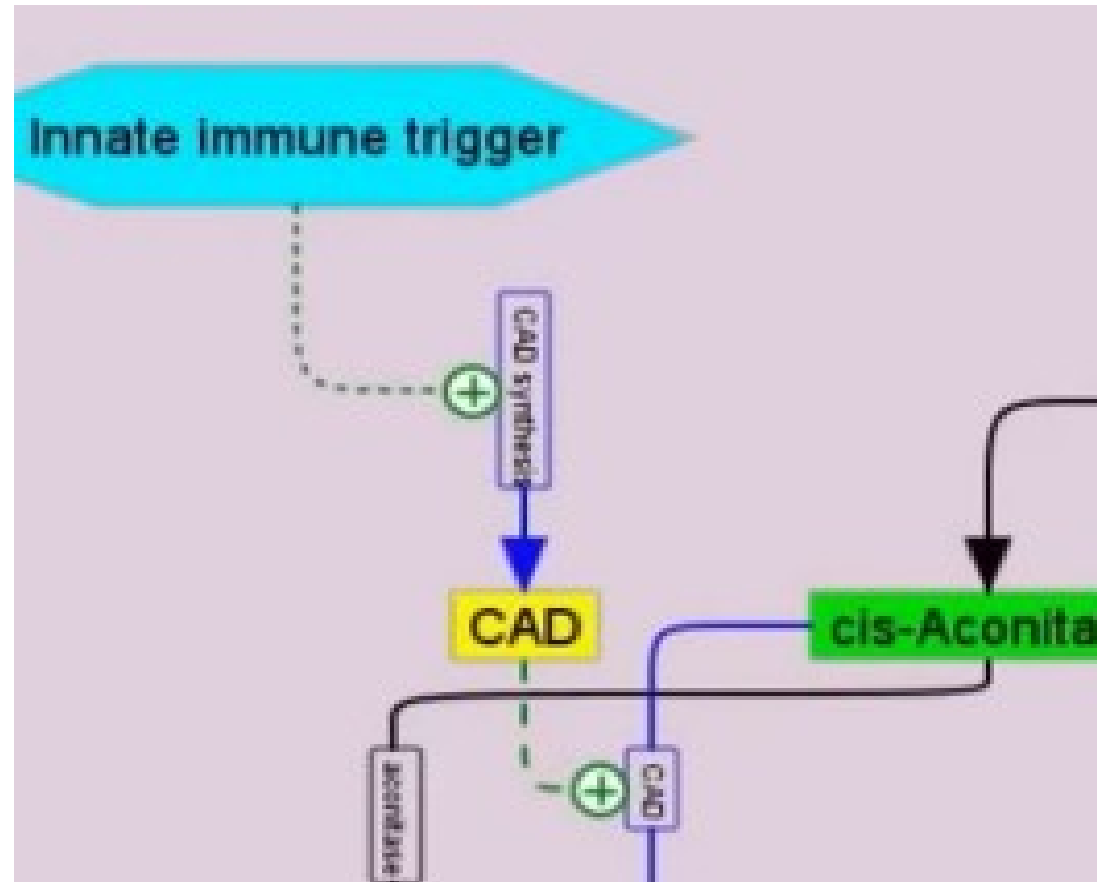


# Aller Übel Anfang

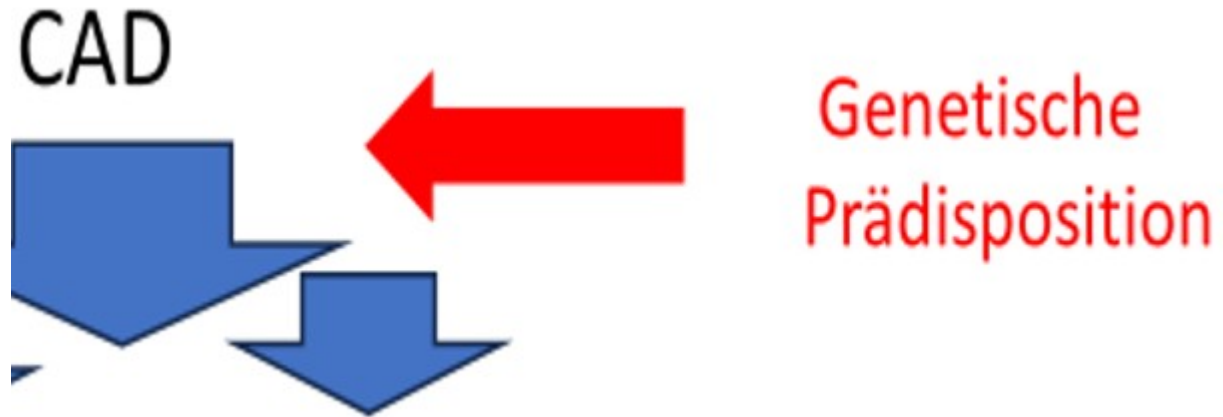
OMF



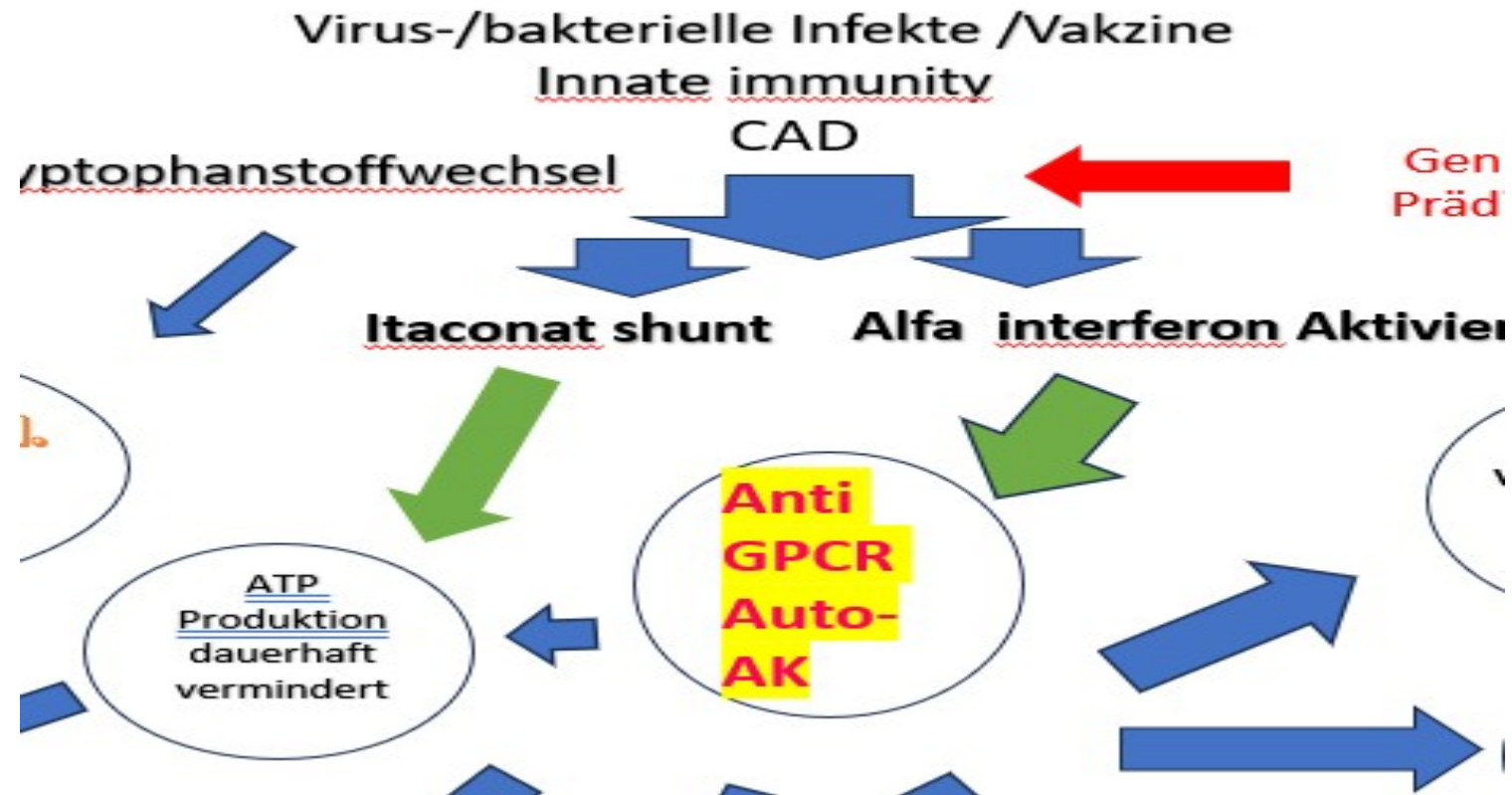
# CAD



# Genetische Prädisposition



# Warum kommt es zur Bildung von GPCR Auto-AK?



CPCR Auto-AK bei Post Vac 10/150  
 9 Positiv , 1 Patientin GPCR AAK negativ  
 anti FGF 3 positiv !

E		pos							
E	pos	pos							
E	pos	pos				pos			
E	pos	pos	pos	pos				pos	pos
biov	pos	pos	pos			pos			
E NEG	anti FgF3	nachgewiesen							
E	pos	pos				pos			
EPV	pos	pos		pos		pos			
E	pos	pos				pos			
E	pos	pos		pos		pos			

# Also

MECFS/PostCovid/PostVac/Post andere

Sind alle dieselbe **Autoimmunerkrankung ( M35.9 G)**

bedingt durch GPCR Auto-AK

Sie kann nur mit neutralisierenden Therapien( BC 007)  
(Ronapreve)

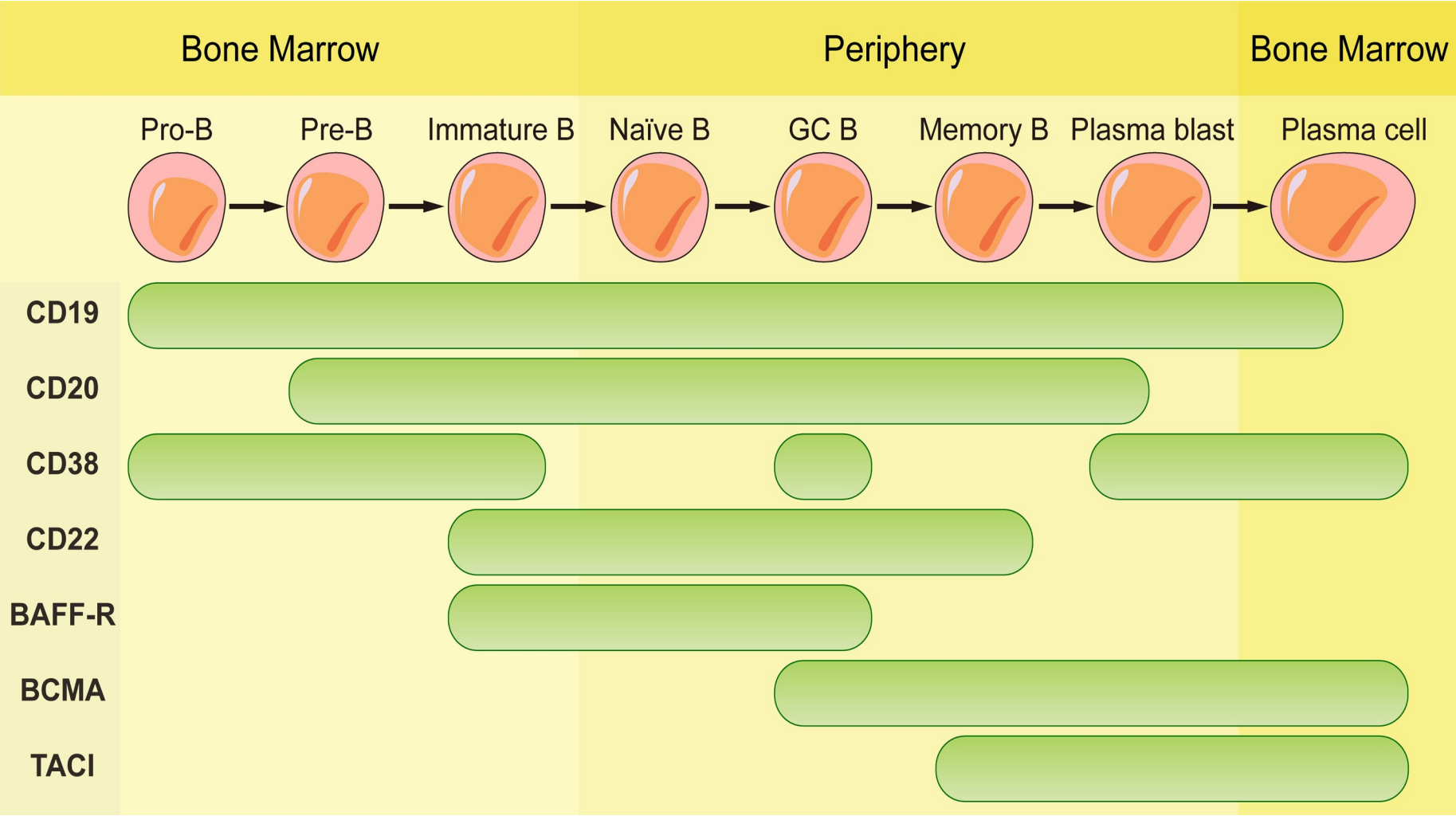
(nicht mit normalen Immunsuppressiva)

oder B-Zell depletierende Therapien behandelt werden

z.B **Rituximab** oder **Belimumab**



Target and technology	Drug	FDA-approved diseases
Chimeric anti-CD20 mAb	Rituximab	Rheumatoid arthritis; Granulomatosis with polyangiitis; Microscopic polyangiitis; Pemphigus
Humanized anti-CD20 mAb	Ocrelizumab	Relapsing and progressive multiple sclerosis
Fully human anti-CD20 mAb	Ofatumumab	Relapsing multiple sclerosis
Humanized anti-CD19 mAb	Inebilizumab	Neuromyelitis optica spectrum disorder
Fully human anti-BAFF mAb	Belimumab	SLE; Lupus nephritis



# Die Rituximab Tragödie

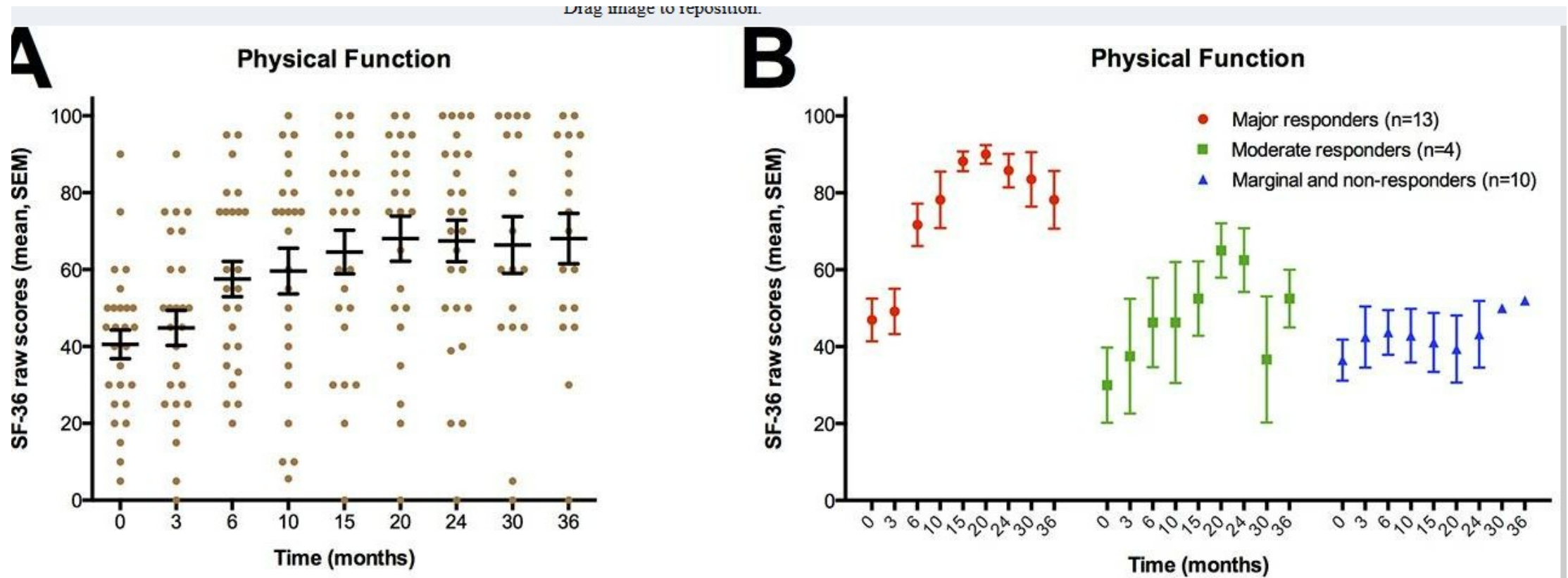
Fluge und Mella

2011

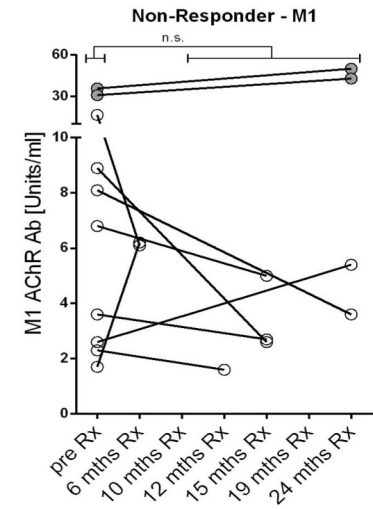
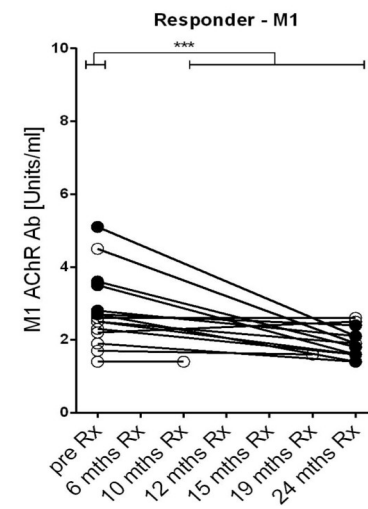
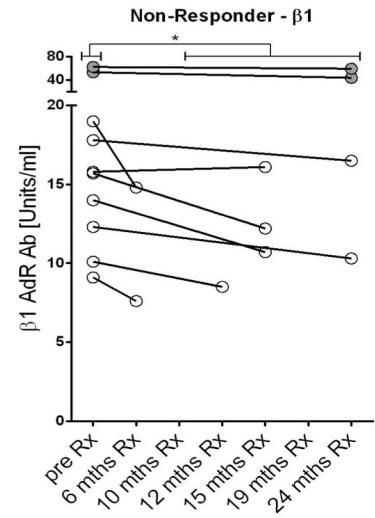
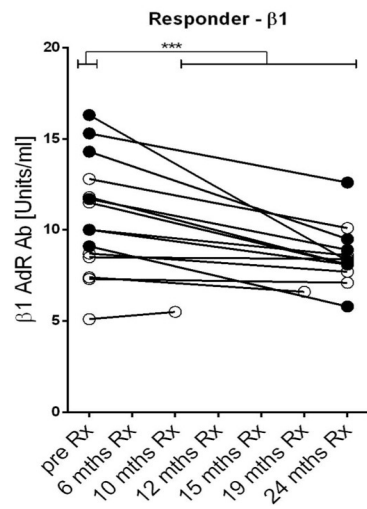
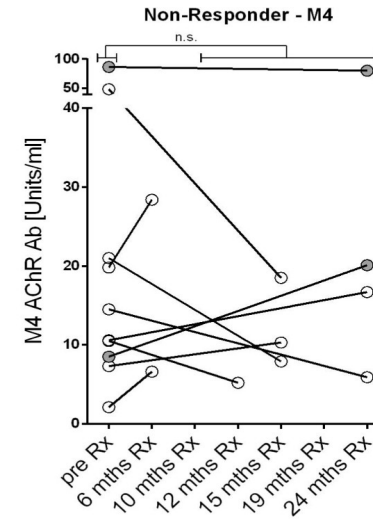
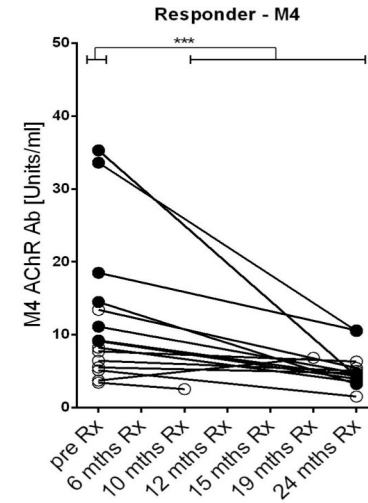
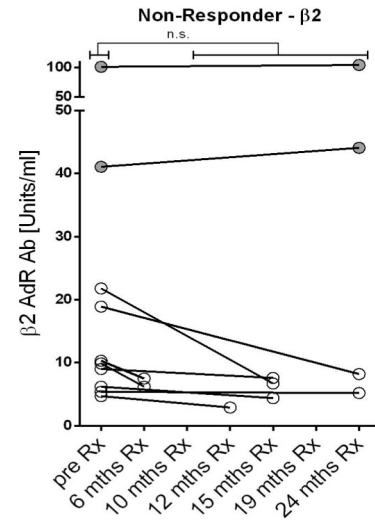
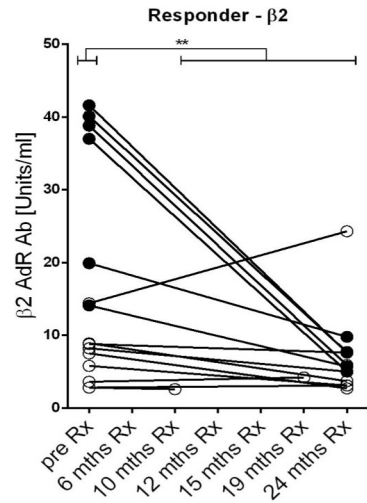
2015

2019

# Scores from KTS 2 during rituximab treatment



# Verhalten der GPCR Auto-AK unter Rituximab in der KTS 2 Studie



Zitat Frau Prof .Scheibenbogen Bericht Cort Johnson

**2021 IACFS/ME Conference**

„She proposed that the reduction of the maintenance dose in the Phase III trial, though, may have doomed the trial. The Phase II trial used maintenance infusions at the rate of 500 mg/m<sup>2</sup> (maximum 1,000 mg) at 3, 6, 10, and 15 months follow-up. The Phase III trial used a fixed dose of 500 mg at 3, 6, 9, and 12 months. Scheibenbogen reported the fixed-dose used was caused by financial problems“

Sie meint das die Dosisreduktion der Erhaltungsdosis in der Phase III Studie, diese zum Scheitern verurteilt hat .

In der kleinen Studie KTS2 wurden 500mg/m<sup>2</sup> als Erhaltungsdosis nach 3,6,10 und 15 Monate gegeben.

Dagegen in der Phase III nur 500mg absolut in den Monaten 3,6,9,12.

Die Fixdosis wurde so festgelegt wegen finanzieller Probleme.

# Immunadsorption ?

## Scheibenbogen 2023

Abfall der GPCR aber Wiederanstieg

Schluss: IA + B Zeldepletierende Therapie (z.B. ofatumumab)

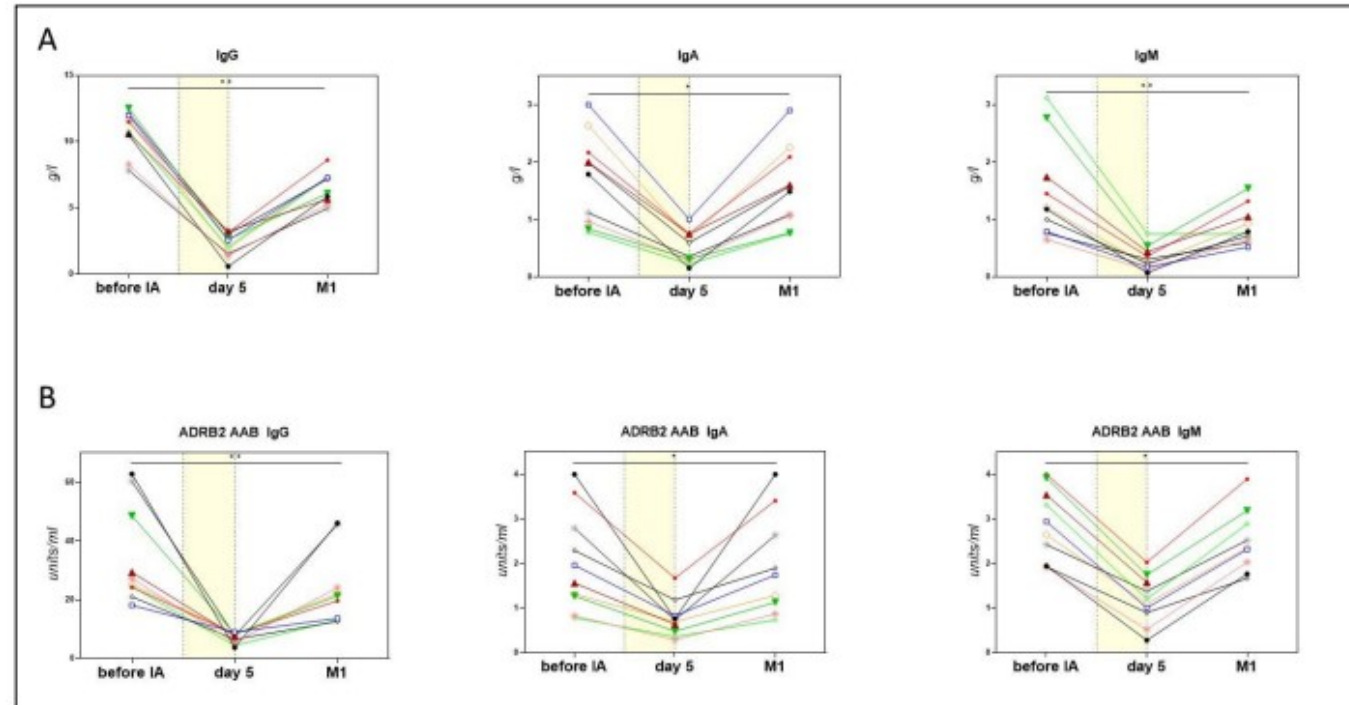
Anfang Studie?????

## Jena 2023

Abfall der GPCR aber Wiederanstieg

Schluss: Rituximab.!!!

# GPCR AAK Verlauf nach Immunadsorption Scheibenbogen



**Figure 1: (A) Levels of IgG, IgA, IgM before IA, the morning before the 5th IA and 4 weeks after IA (B) Levels of ADRB2 AAB IgG, ADRB2 AAB IgA, ADRB2 AAB IgM before IA, the morning before the 5th IA and one month (M1) after IA. The period of IA treatment is indicated by a yellow area. ADRB2 AABs were determined by CellTrend GmbH, Luckenwalde, Germany using**



# Und Jetzt ?

Scheibenbogen. Studie IA+Ofatumumab

OMF LDN +Pyridostigmin???

Iwasaki Paxlovid ???

Metares Tripeltherapie  
LDN,Nikotin,Pyridostigmin

Oder doch Behandlung mit AK gegen COVID

**Ronapreve**

Drei Patienten genesen!!!

Nach **einer** Woche komplette Remission!!!