



# 50 YEARS ANNIVERSARY



Hartmut Porzig

**Fünfzig Jahre Friedbühlstrasse  
oder  
Die Pharmakologie ist lang, doch kurz ist unser Leben**

Auf fünfzig Jahre Friedhofsblick  
Schaut jetzt die Pharmakologie zurück.  
Doch trotz der Aussicht der makabren  
Wird niemand mit dem Schicksal hadern,  
selbst wenn dem schlichten Institut  
der Denkmalschutz noch fehlen tut.  
Nur manchmal denken noch die Veteranen  
Die früher hier zusammenkamen:  
Wie war die Fassade doch vordem  
Mit blauen Kacheln doppelt schön!  
Doch soll nichts Äusserliches unsere Sicht bestimmen  
Denn die wahren Werte liegen innen!  
Wer zählt die Forscher, nennt die Namen  
Die alle hier zusammenkamen,  
um mit Genie und Fleiss vor allen Dingen  
die Pharmakologie voran zu bringen:  
Wilbrandt, Bickel, Simon, Reuter  
Mit allen ging der Fortschritt weiter.  
Auch Assistenten, Doktoranden  
Und all, die mehr im Schatten standen  
Sie mühten sich an diesem Ort  
Und pflanzten sich durch Papers fort.

Jedoch am Anfang war hier nicht das Wort,  
Sondern der Membrantransport.  
In roten Zellen, Herzen, Häuten  
Wurde er von vielen Leuten  
Mit grossem Aufwand, wie besessen  
Ausschliesslich analog vermessen.  
Nur manchmal sprach man auf den Fluren  
Gelegentlich von Zellkulturen  
Und - man glaubt es nicht – noch kaum  
War Molekularbiologie ein Traum.  
Vom Internet noch keine Spur  
Und für die gesamte Lit'ratur  
Gab es als Quelle, ach herrje,  
Nur den Gang zur USB.  
Die Zeit verging, mit einem Mal  
wurde alles digital.  
Ein neuer Rechner kam ins Haus

Und füllt ein ganzes Labor aus.  
Der konnte zudem, ohne Geizen  
Fast das ganze Insti heizen.  
Kanalarbeiter sah man dann  
sich mühen um die Zellmembran  
und plötzlich sah man wunderschön  
in der Membran die Türn aufgehen.  
Doch Andre über beide Ohren  
Verliebten sich in Rezeptoren  
Für Hormone und Transmitter  
Doch blieb ihr Wissen noch recht schütter.  
Ein wenig später zur Verzierung  
Wir lernten Fluoreszenzmarkierung  
Und sahen die Welt mit einem Mal  
Ganz erstaunlich konfokal.  
Eine neue Richtung nahm das Schiff  
Als ein anderer Chef ins Ruder griff.  
Am Anfang wurde ziemlich laut  
Im Institut viel umgebaut.  
Auch Membrantransporte, das war klar  
Fand er nicht so wunderbar.  
Dafür stieg er kräftig in die Hose  
Für Entzündung und Apoptose  
Führt seine Gruppe auch mit Fleiss  
Zu manchem schönen Forschungspreis.

So könnte ich-schon alt an Jahren  
Noch eine Weile weiterfahren.  
Doch ziemt es sich an diesem Ort  
Zu schliessen mit `nem Dichterwort:  
Alles vergänglich ist nur ein Gleichnis  
Das Unzulängliche, hier wards Ereignis  
Das Unvergleichliche, hier wird's getan,  
denn nur die Wissenschaft bringt uns voran.





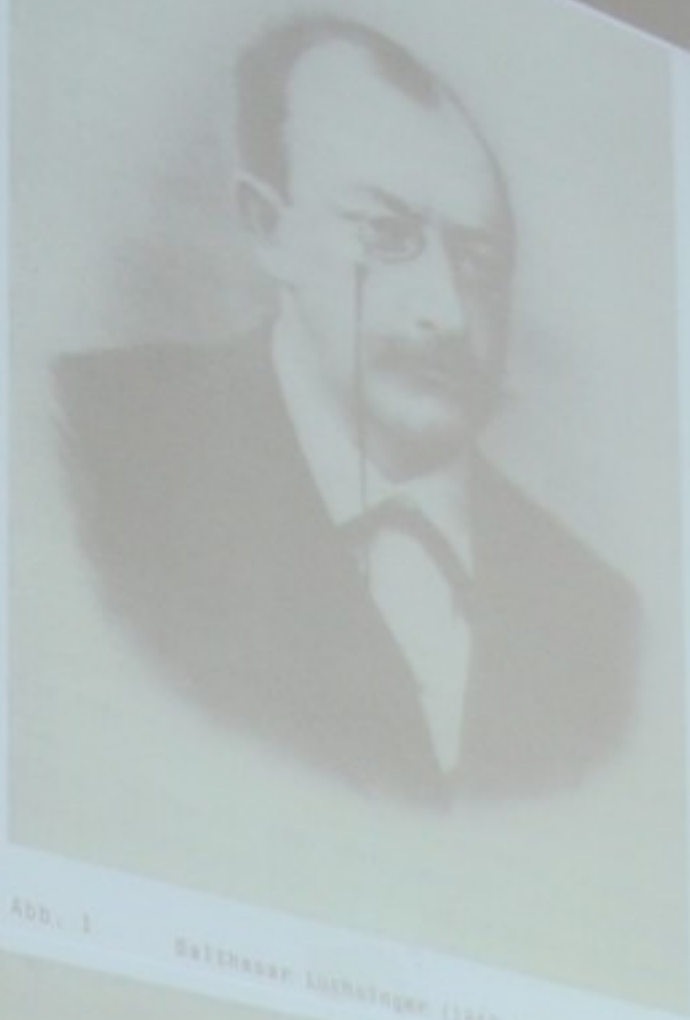


Abb. 1  
HEINRICH LUCHOW (1868-1948)

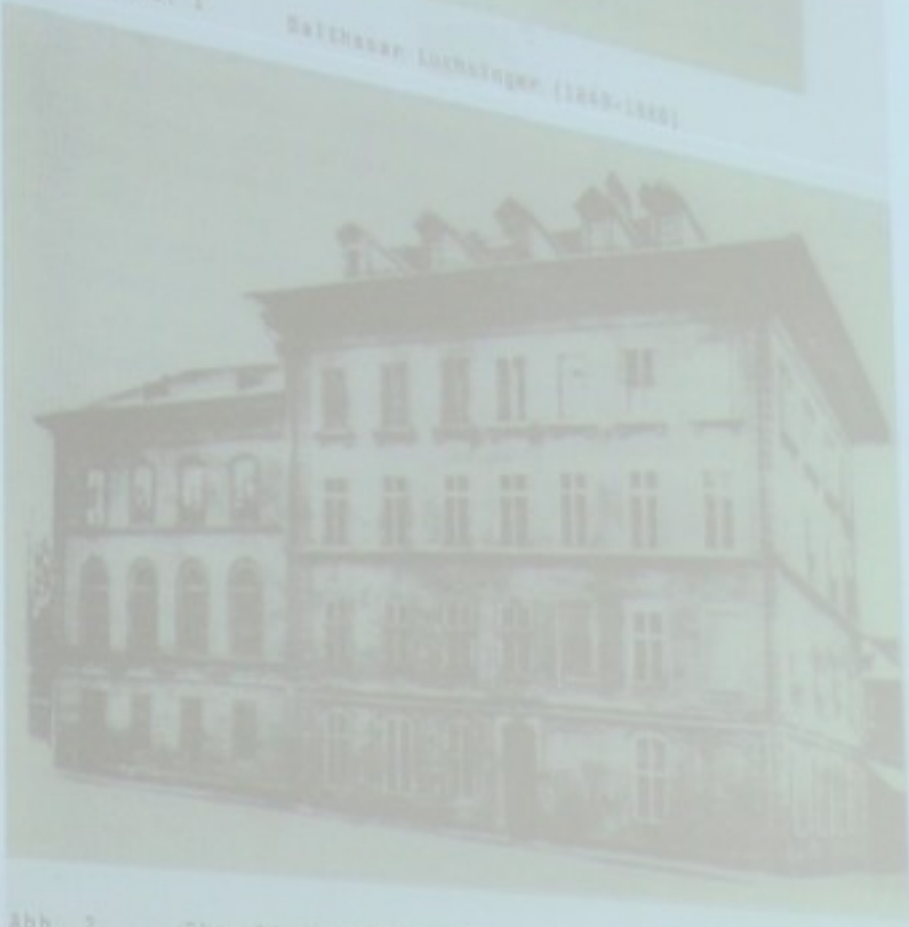


Abb. 2  
Ehemaliges Gebäude der Staatsapotheke, Pharmakologisches und Toxikologisches Institut im 3. Stockwerk.






**The Fruitful Cross-Talk between  
Pharmacology and Cellular Microbiology**  
- 50 years of  
Pharmacology in  
Bern -

**Klaus Aktories**

Institut für Experimentelle  
Klinische Pharmakologie  
und Toxikologie

Universität Freiburg





Ingo Just  
(Hannover)  
Holger Barth  
(Ulm)  
Roland Benz  
(Würzburg)  
Wolf-Dieter Hardt  
(Zürich)



























... relevance in delivery  
of drug molecules

Julijana Kristl

Bern Institute for Pharmacology



# Drug Discovery in Academia

1 Historical considerations

2 Technologies

3 Products



- Show attractiveness
  - Provide medical services in collaboration with internal medicine specialities
  - Be strong in one of the mentioned research fields
  - Look for reimbursement of typical tasks in clinical pharmacology.
- TDM....



- Financially not im...
- Measures
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- specialities
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### PI3Ks mediate TNF $\alpha$ -induced neutrophil cell death

Barbara Geering and Hans-Uwe Simon  
Department of Pharmacology, University of Bonn, Germany  
barbara.geering@uni-bonn.de

#### 1 Aim of this study

Neutrophils are the first line of defense against invading pathogens. The mechanical barrier of mucus is coupled with cilia and contractility and involves the generation of reactive oxygen species (ROS). In the resolution phase of inflammation, activation of TNF receptor family members is known to mediate apoptosis.

In order to gain insight into the molecular mechanisms of TNF $\alpha$ -induced neutrophil apoptosis, we investigated the signaling events downstream of TNFR1, with focus on the role of PI3Ks.

#### A Inhibition of TNF $\alpha$ -stimulated apoptosis

Neutrophil apoptosis is inhibited by TNF $\alpha$  in a dose-dependent manner. This effect is mediated by TNFR1 and involves the generation of ROS. In the resolution phase of inflammation, activation of TNF receptor family members is known to mediate apoptosis.

#### B PI3Ks are activated

PI3Ks are activated by TNF $\alpha$  in a dose-dependent manner. This effect is mediated by TNFR1 and involves the generation of ROS. In the resolution phase of inflammation, activation of TNF receptor family members is known to mediate apoptosis.

#### 3 Conclusions

Class IA PI3Ks mediate apoptosis of human neutrophils. PI3Ks are constitutively bound to TNFR1. PI3Ks are activated by TNF $\alpha$  upon TNFR1 activation. PI3Ks control ROS generation in TNF $\alpha$ -stimulated neutrophils. PI3Ks control ROS generation in TNF $\alpha$ -stimulated neutrophils. PI3Ks control ROS generation in TNF $\alpha$ -stimulated neutrophils.

### Thymic stromal lymphopoietin (TSLP) stimulates eosinophils to release mitochondrial DNA and eosinophil cationic protein

Mehboob Muneer, Shida Yousefi, Christina Mera-Böckle, Hans-Uwe Simon, Dagmar Simon  
Institute of Pharmacology and Department of Dermatology, University of Bonn

#### Background

Eosinophils play an important role in host defense, immunoregulation and tissue remodeling. Recently, the release of mitochondrial DNA together with toxic granule proteins forming eosinophilic extracellular traps (EETs) has been reported. EETs are a potent mechanism of killing bacteria and have been observed in infectious intestinal diseases. TSLP is produced by epithelial cells at barrier surfaces including the intestine, airways and skin. Elevated TSLP expression has been found in atopic diseases such as atopic dermatitis, bronchial asthma and allergic rhinitis.

#### Aims

We sought to investigate the effect of TSLP on eosinophils to release EETs. The extra- and intracellular mechanisms involved as well as TSLP receptor (TSLPR) expression in vitro and in vivo.

#### Methods

Human eosinophils were isolated from peripheral blood. For DNA release assay, cells were taken on cover slips, incubated with TSLP or control, fixed and analyzed by confocal laser scanning microscopy. TSLPR expression was measured by immunofluorescence staining. Eosinophil degranulation was measured by flow cytometry. TSLP receptor expression was measured by immunofluorescence staining. TSLP receptor expression was measured by immunofluorescence staining.

#### Results

TSLP directly and specifically activates eosinophils to release DNA.

TSLP mediated EET release is adhesion dependent but independent of cell death.

EETs consist of DNA and ECP (eosinophil cationic protein).

TSLP stimulates mitochondrial DNA release by eosinophils.

TSLP stimulates eosinophil degranulation.

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### Neutrophil release mitochondrial DNA to form neutrophil extracellular traps in the absence of cell

Shida Yousefi, Cristina Mihalache, Evelyn Kozłowski, Ines Schmitt & Hans-Uwe Simon  
Institute of Pharmacology, University of Bonn, Germany

#### Background

Neutrophils release mitochondrial DNA to form neutrophil extracellular traps (NETs) in the absence of cell death. This process is mediated by the release of mitochondrial DNA together with toxic granule proteins forming neutrophil extracellular traps (NETs). NETs are a potent mechanism of killing bacteria and have been observed in infectious intestinal diseases. TSLP is produced by epithelial cells at barrier surfaces including the intestine, airways and skin. Elevated TSLP expression has been found in atopic diseases such as atopic dermatitis, bronchial asthma and allergic rhinitis.

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We sought to investigate the effect of TSLP on neutrophils to release NETs. The extra- and intracellular mechanisms involved as well as TSLP receptor (TSLPR) expression in vitro and in vivo.

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# PI3Ks mediate TNF $\alpha$ -induced neutrophil cell death

Barbara Gerrits and Hans-Gert Simon  
Department of Pharmacology, University of Bonn, Germany  
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## 1 Aim of this study

Neutrophils are the first line of defense against invading pathogens. The appropriate number of neutrophils is essential for host defense and excessive generation of reactive oxygen species (ROS). In the resolution phase of inflammation, activation of TNF receptor family members is needed for neutrophil apoptosis.

In order to gain insight into the molecular mechanisms of TNF $\alpha$ -induced neutrophil apoptosis, we investigated the signaling events downstream of TNFR1, with focus on the role of PI3Ks.

## 2 Results

### A Inhibition of p38 or PI3Ks in TNF $\alpha$ -stimulated neutrophils



### B PI3Ks are constitutively bound and activated by p38 upon TNF $\alpha$ stimulation



## 3 Conclusions

Class III PI3Ks mediate apoptosis of human neutrophils. PI3Ks are constitutively bound to TNFR1. PI3Ks are activated by p38 upon TNF $\alpha$  stimulation. p38/TNFR1 controls PI3K generation in TNF $\alpha$ -stimulated neutrophils. p38/TNFR1 pathway increases neutrophil apoptosis without involvement of ROS. PI3Ks are constitutively bound to TNFR1.

## Background

Neutrophils play an important role in host defense, immunity and tissue remodeling. The release of mitochondria together with toxic granules forming neutrophil extracellular traps (NETs) has been observed in infectious diseases. NETs are a potent microbicidal bacteria and have been observed in infectious diseases. NETs are a potent microbicidal bacteria and have been observed in infectious diseases. NETs are a potent microbicidal bacteria and have been observed in infectious diseases.

## Aims

We sought to investigate the role of TNF $\alpha$  on neutrophils. NETs, the auto- and cross-linking mechanisms involved in NETs, the auto- and cross-linking mechanisms involved in NETs, the auto- and cross-linking mechanisms involved in NETs.

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