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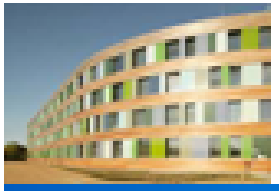
Fakultät Umweltwissenschaften – Institut für Hydrobiologie

Challenges and opportunities of post market surveillance: fate and effects monitoring

Dirk Jungmann



Environmental risk assessment in the authorization procedere

Umwelt Bundes Amt

Pre market surveillance

administrative information and scientific documentation

Marketing approval

benefit-risk- analysis

Post market surveillance (pharmakovigilance)

collection and scientific evaluation of information on suspected adverse reactions related to the use of a medicinal product etc.

Environmental risk assessment required for all new applications (technical guidances available)

Obligation to report on environmental problems of veterinary medicinal products

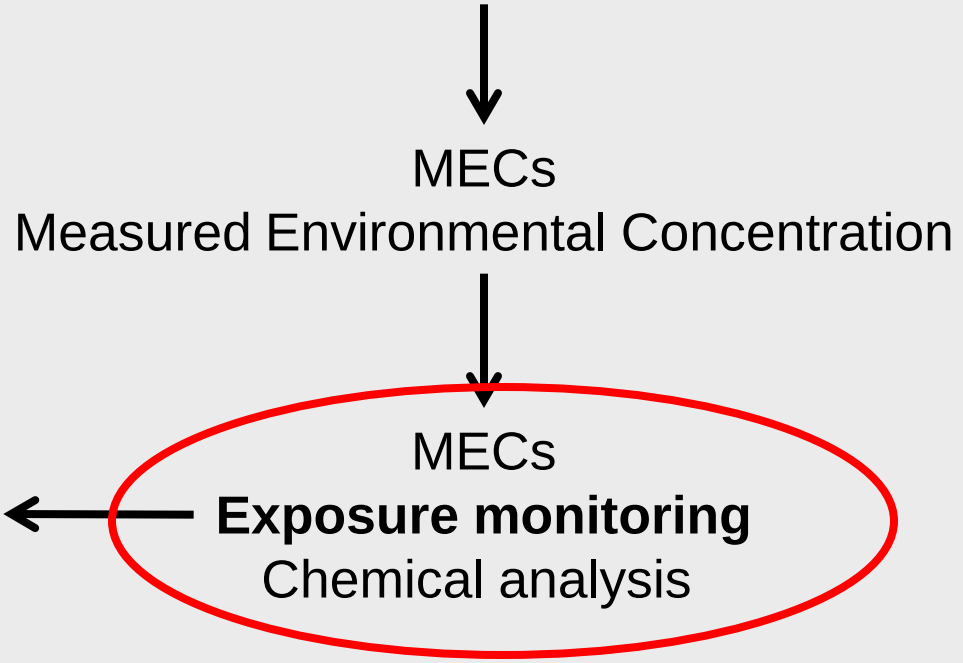
Environmental problems?

Hazard of a compound

Effect analyses

Occurrence of a compound

Environmental concentrations



Definition

Monitoring

… in general monitoring is a topic describing a systemic recording, observing or control of events or processes

Biomonitoring records and observes systematically .

- regularly repeated observation of the condition and inventory of plants and animals and their communities to determine the environmental quality.

retrospective

Effect monitoring <- toxicodynamic

(aus Van der Oost et al. 2003; Rüdel et al. 2007)

Definition

Monitoring

Toxicodynamic

.... is the study of the physiological effects of chemicals (VMPs) on the organism.

How does the chemical act on the organism?

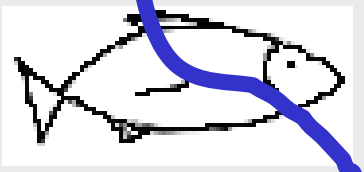
Biomonitoring is “something or someone who warns an overseer” (Rüdel et al. 2007)

Sampling site upstream

Pollution

Biomarker

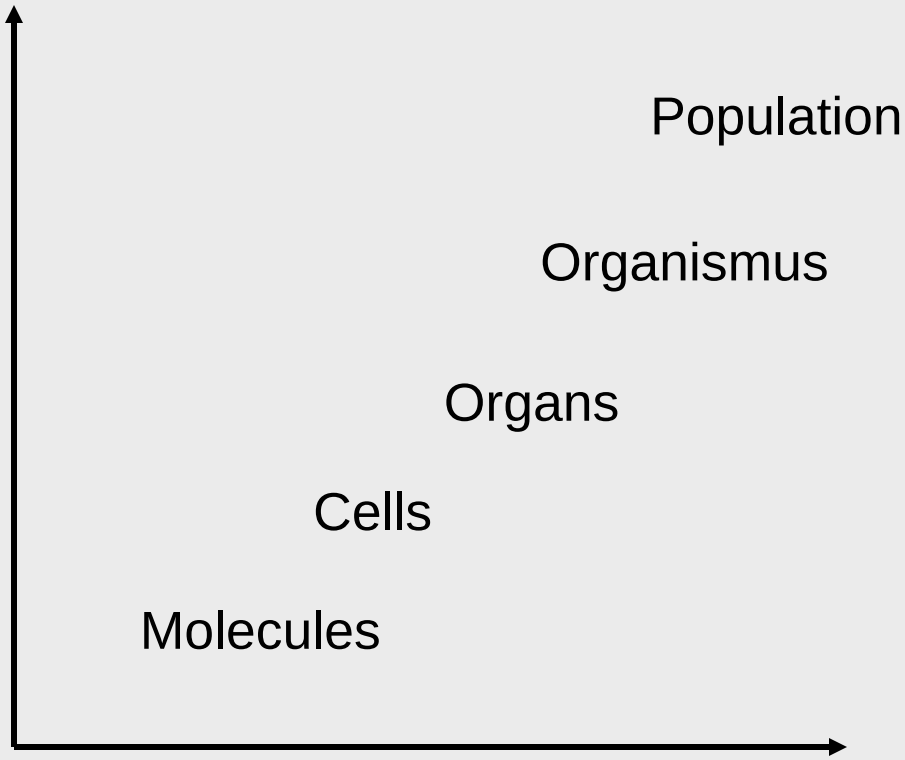
Sampling site downstream

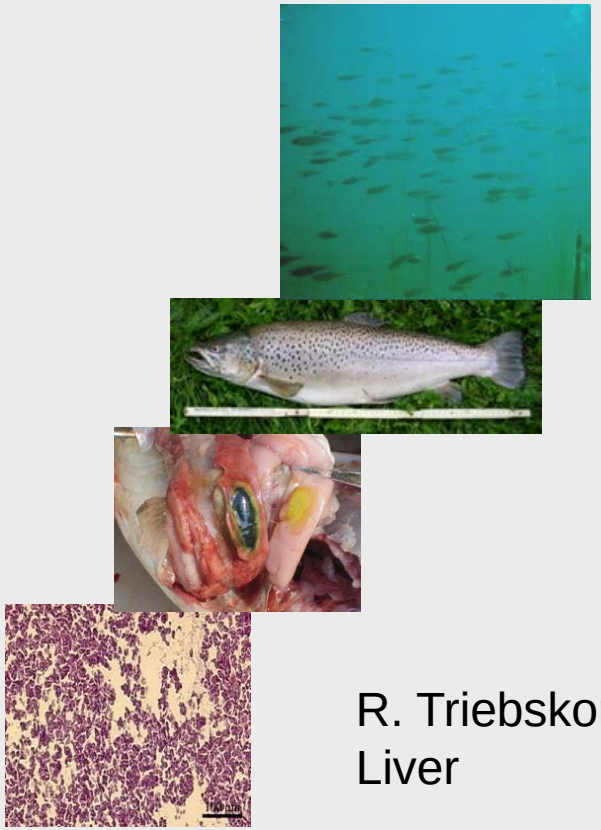


Level of integration

Observation of different biological tier:

molecular -> population

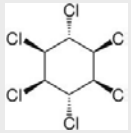




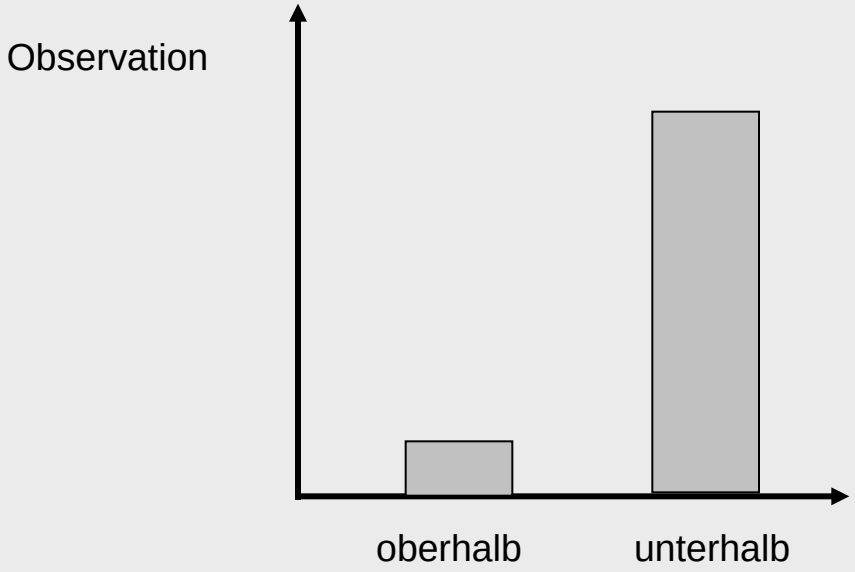
R. Triebskorn
Liver

Cause - Response - Relationship

Observation - general: z.B. CYP 450 (Biomarker)

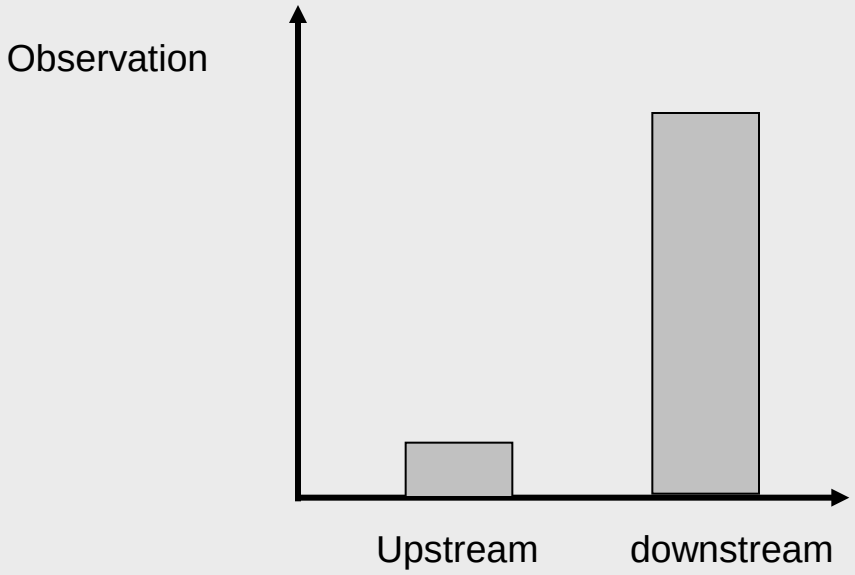


Organism **Observation** Significant effect



Biomonitoring is “something or someone who warns an overseer”
(Rüdel et al. 2007)

Cause - Response - Relationship



CYP 450 (Biomarker) indicates pollution

but only a general

Cause - Response - Relationship

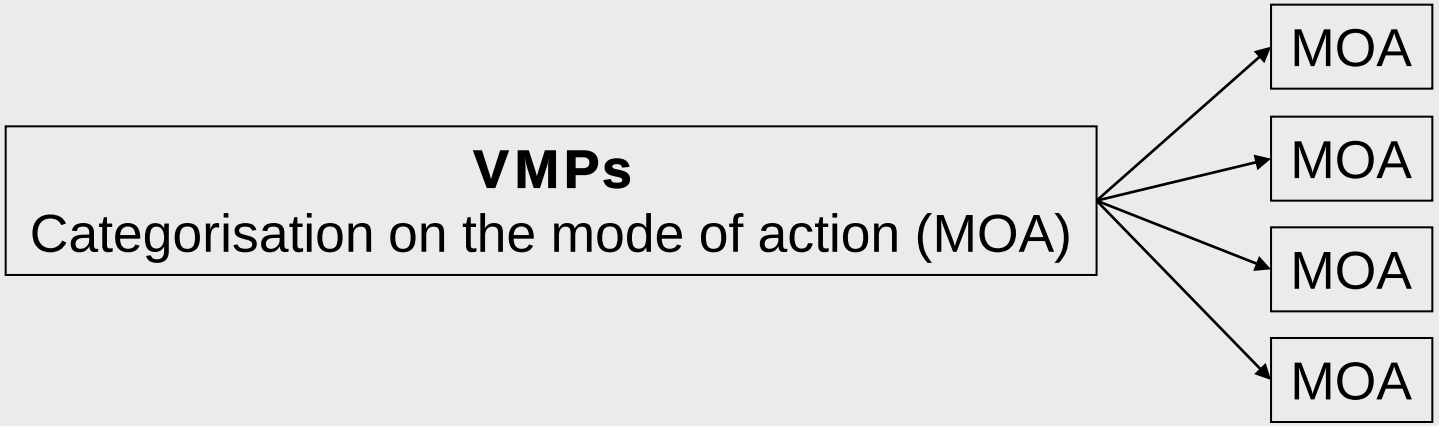
Cause - Response - Relationship

Toxicodynamic

…. is the study of the physiological effects of chemicals (pharmaceuticals) on the organism.

VMPs

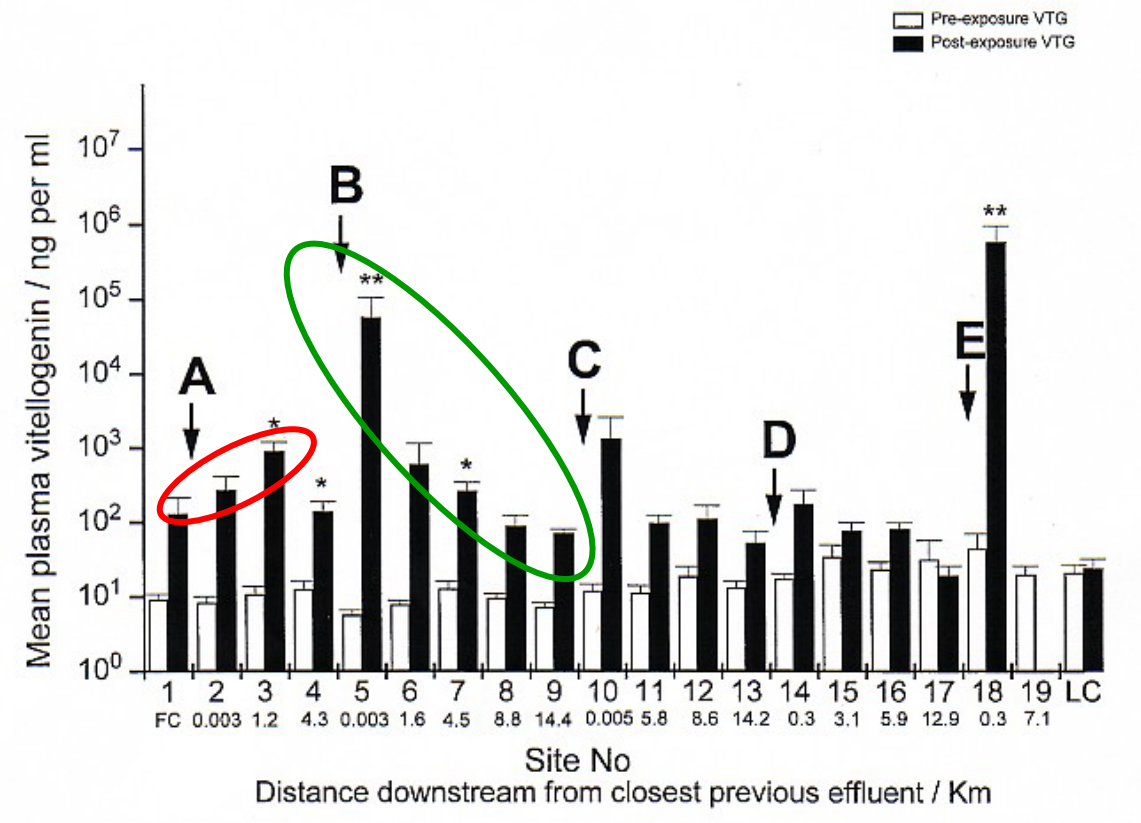
Topic of **application** (Pesticide, Biocide, etc.)



Lessons from biomarker

Signal

- Special: Vitellogenin-content in the blood of male fish effectmonitoring



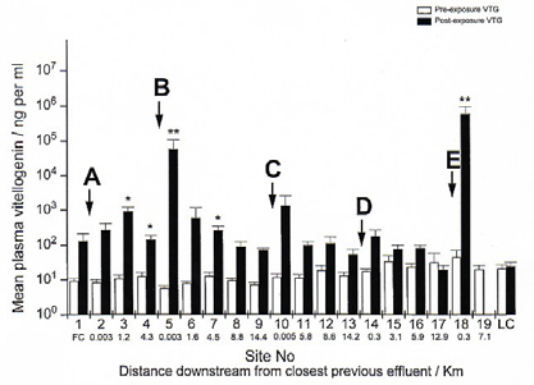
Harris et al. 1996

Lessons from biomarker

Signal

- Special: Vitellogenin-content in the blood of male fish

Effectmonitoring



Endocrine effective compounds → Effect

Harris et al. 1996

Cause - Response - Relationship

Responsible compounds?

- Atrazin
- DDT
- DDE
- DDD
- Dichlovos
- Dieldrin
- Dimethoat
- Diuron
- Endosulfan
- Lindan
- Malathion
- Parathion-methyl
- Simazin
- Trifluralin

- Nonylphenol
- 4-Nonylphenol
- 4-tert-Oktylphenol
- 4-tert-Pentylphenol
- Bisphenol A

Pharmaceuticals

- Medroxyprogesteron
- Flutamid
- Spironolacton
- 17a-Ethinylestradiol
- Hydroxyprogesteroncaproat
- Mestranol
- Tamoxifen
- Megestrol
- b-Sinosterol
- Aminogluthethimid
- Fosfestrol
- Testosteron
- Östradiolvalerat
- Letrozol

Landesumweltamt Brandenburg (2000)

No detection of a field of application! -> pharmaceuticals

Biomonitoring

Complex field to detect pollutants and a challenging task

Application is not the MOA

It is possible to identify areas of concern and need for action

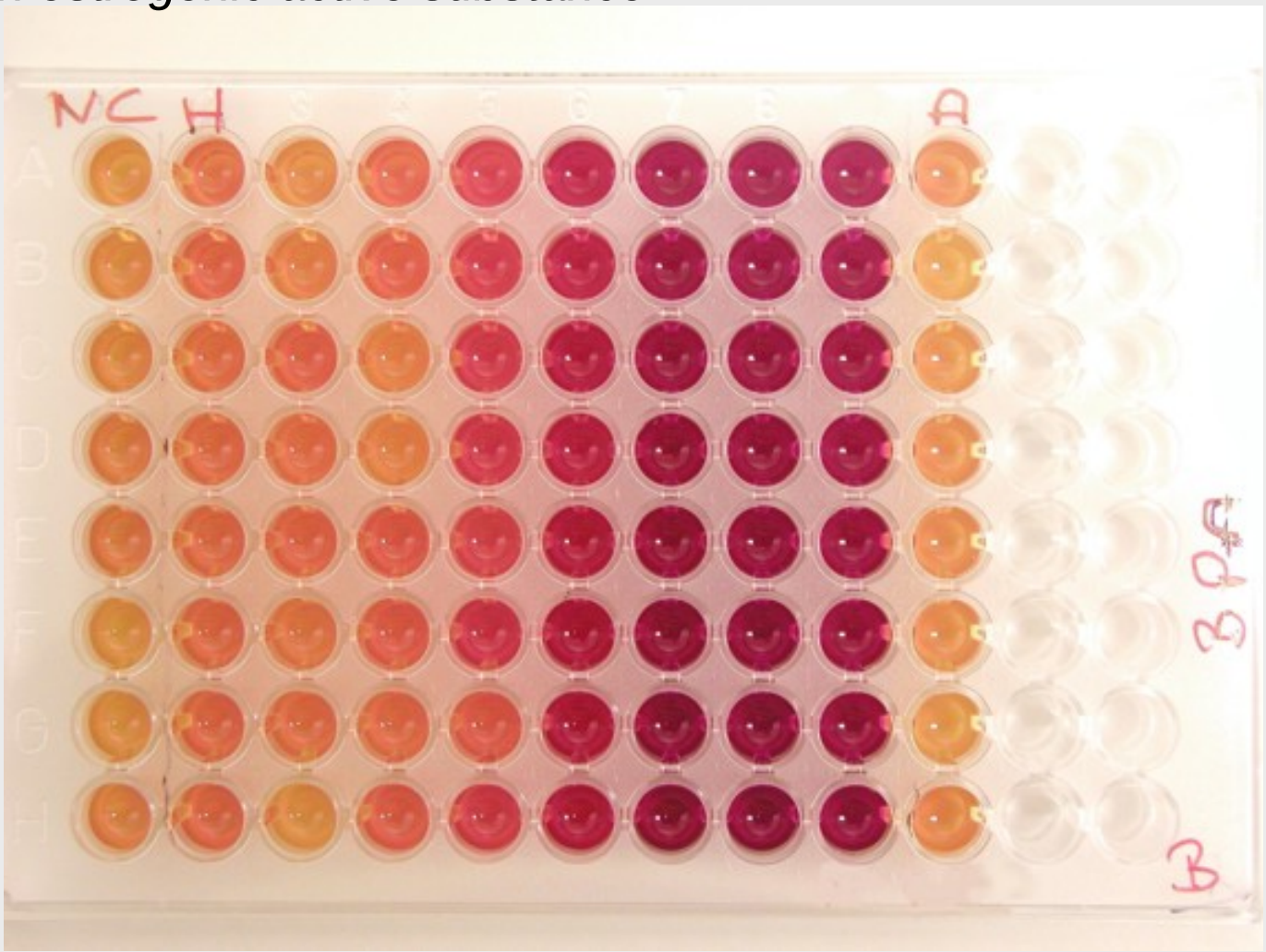
Potentials

- Advantages
  - in contrast to e.g. industrial chemicals the MOA of VMPs is well known
  - methods are available to determine the impact on target molecules -> toxicodynamik

Potentials

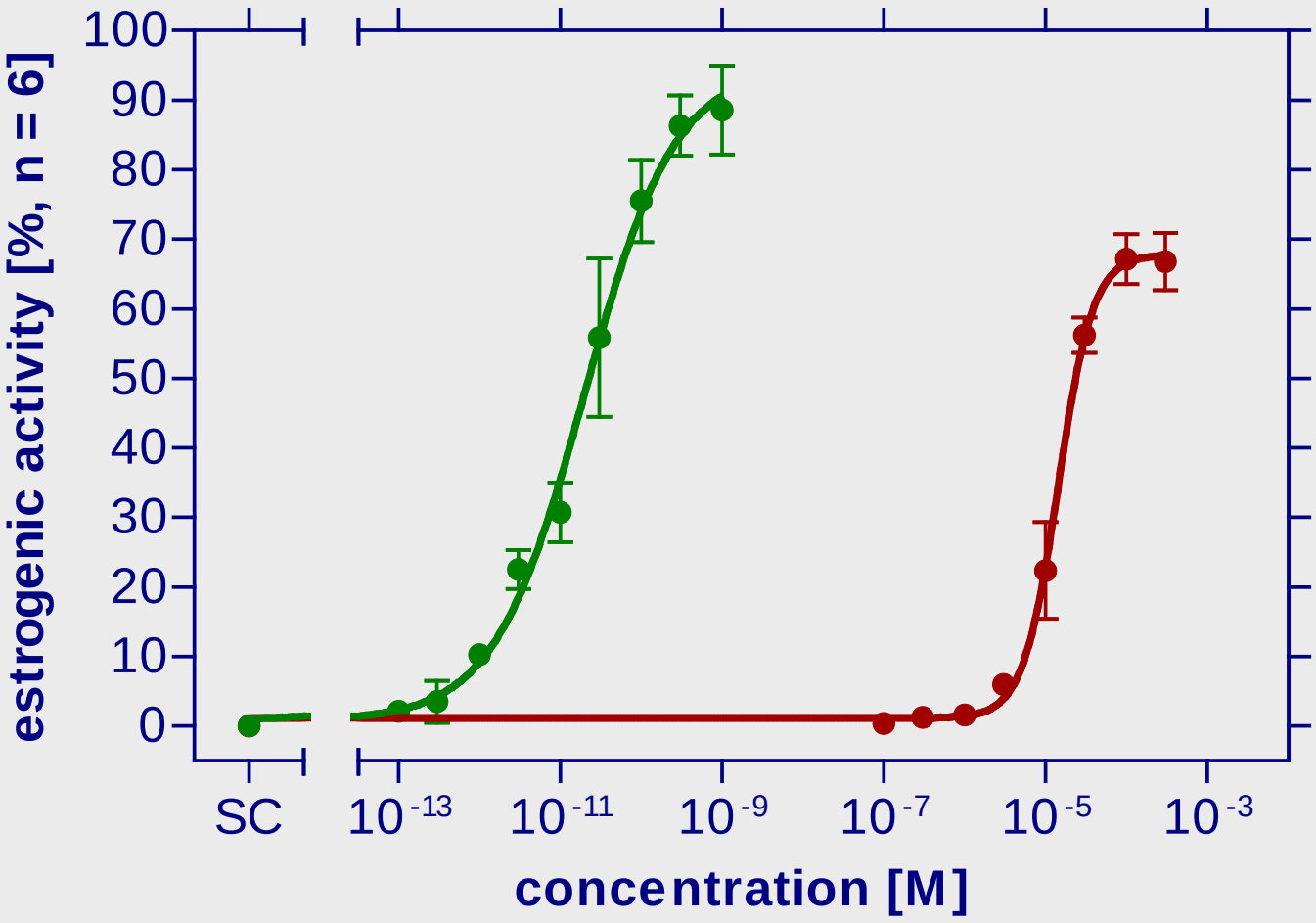
YES or YAS to detect endocrine active substances;

YES with estrogenic active substance



Potentials

Concentration- response relationship: positive control (17ß-estradiol) and estrogenic active substance



Potentials and strategies

Differentiation:

Applications

hypertension, lipid-lowering drugs, analgetica.

MOA

β1-Adreno receptoren blocker (beta blocker)

Inhibition of hydroxymethylglutaryl-CoA-reductase (HMG-CoA-Reductase)

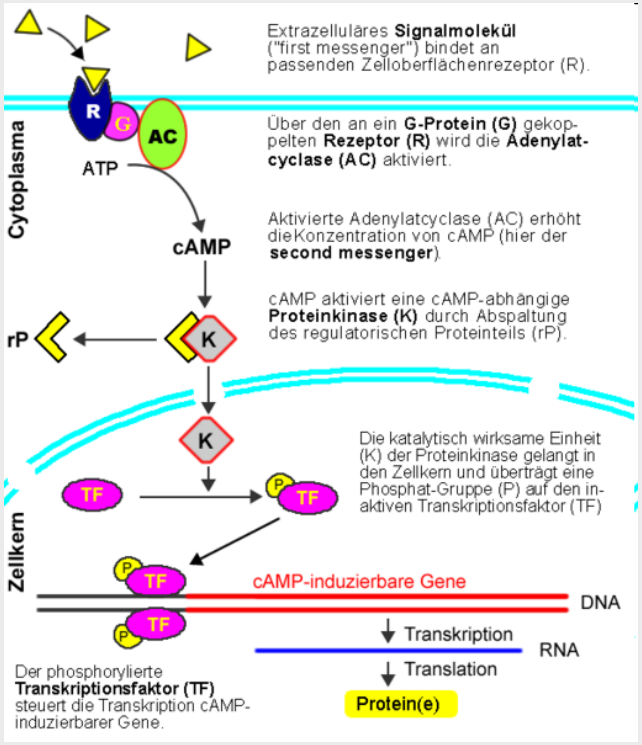
Inhibition of Cyclooxygenases (COX)

Potentials and strategies

hypertension

β1-Adreno receptoren blocker (beta blocker)

Very specific (R) Receptor ; used in pharmaceutical research as screening tool

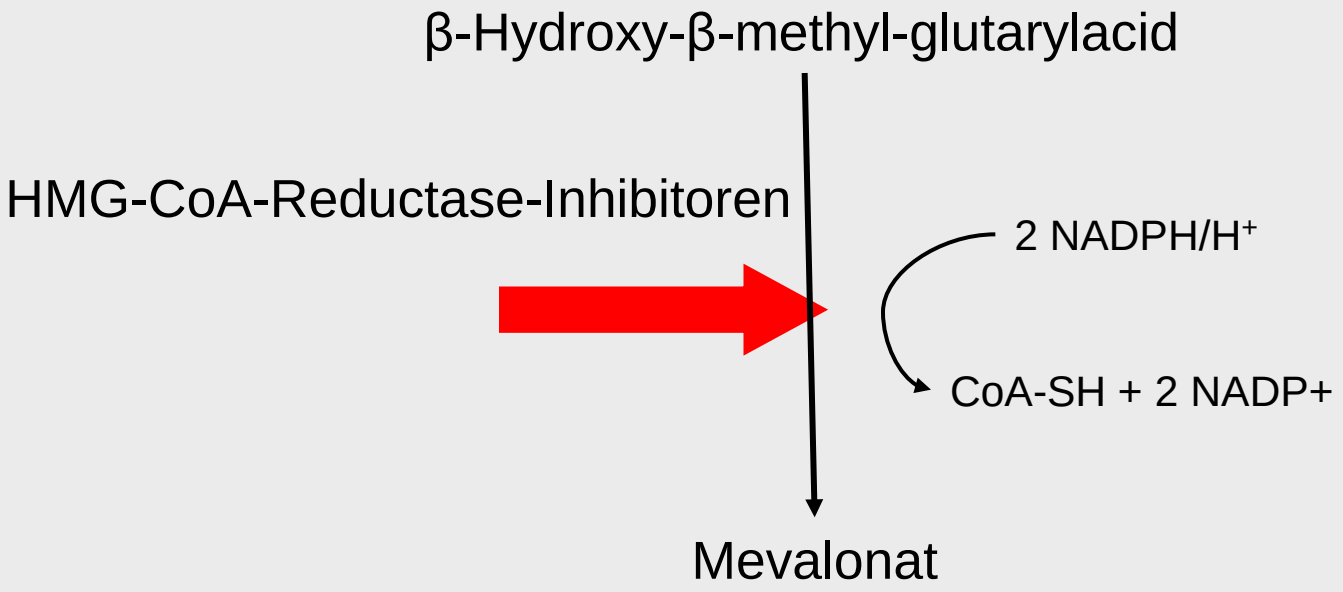


Vereinfacht nach KNIPPERS,R. (2006): Molekulare Genetik, Thieme-Verlag

Potentials and strategies

lipid-lowering drugs – cholesterin synthese

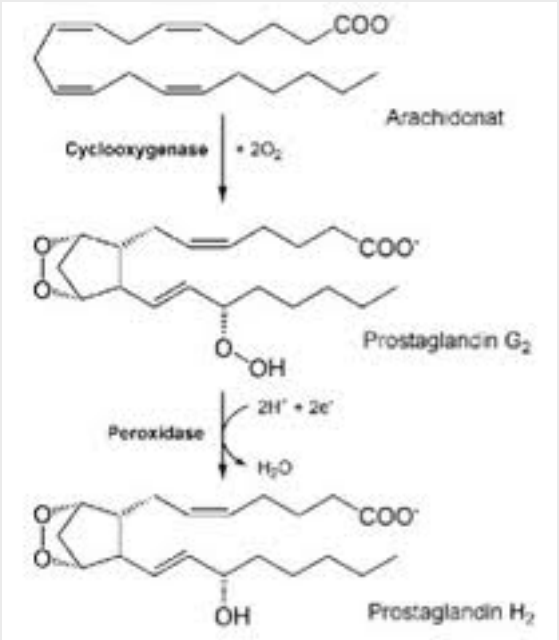
Statine
Atorvastatin
Cerivastatin
Fluvastatin
Lovastatin
Pitavastatin
Pravastatin
Rosuvastatin
Simvastatin



Potentials and strategies

Analgetika – Inhibition of Cyclooxygenase (COX)

ASS
Diclofenac
Ibuprofen



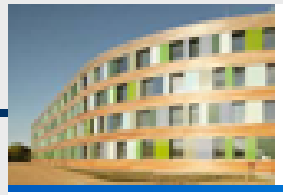
summary

- VMPs must be categorised after the MOA
- *in vitro - m*onitoring with specific biomarker is possible

- *in vivo* – passives monitoring is possible too as detection methods from human medicin are available

Monitoring of VMPs is possible and urgently necessary to get a survey on regions and substances of concern

However validation and some more research is necessary



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Acknowledgement

Thanks to my colleagues

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And for your

attention