

# Chinese version of the DevTox data base and atlas of common malformations

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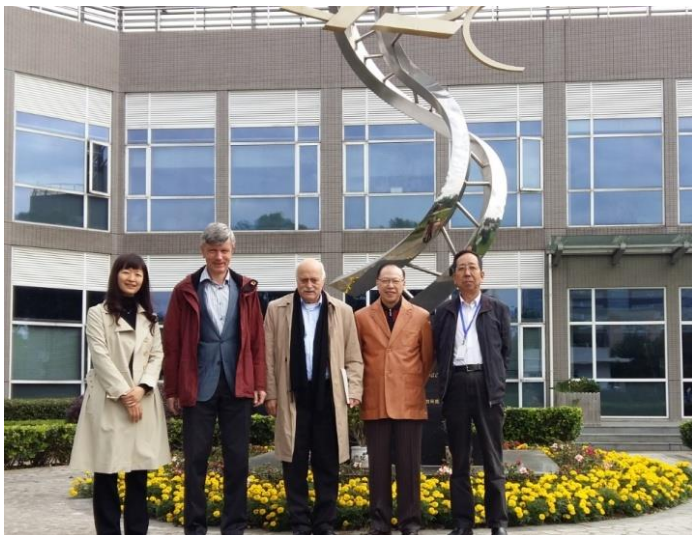
- Brief Introduction
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- New images uploaded
- Malformations induced by Retinoic Acid
- A Chinese book “Atlas of common malformations in Laboratory Rabbit and Rat”



# 8<sup>th</sup> Berlin-Workshop on DevTox Terminology, BfR, Berlin 2014



Participated in 8th Berlin-Workshop on DevTox Terminology Berlin in 2014, and discussed about the possibility for collaboration.



A collaborated project was jointly supported by BfR and Shanghai Science and Technology Committee (STCSM) in 2015

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## 实验动物胚胎发育异常图像数据库的国际化合作建设

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**【摘要】** 实验动物胚胎发育异常图像数据库(DevTox数据库)是面向全球的、非盈利性的、开放共享的发育毒理学资源库, 配有数千张发育异常的图片、说明、术语和统一分类, 极大地促进了发育毒理学研究中形态异常描述术语的统一和规范化。DevTox数据库汇集了欧洲、亚洲发育毒理学界的研究成果, 是一项国际化合作建设项目, 需要各国科学家的共同努力, 将其建设成为最全面的发育毒理学图像资源库。DevTox数据库中文版已于2016年底正式上线, 期待中国科学家为DevTox数据库的更新完善做出贡献。

**【关键词】** DevTox数据库; 发育毒理; 形态; 胚胎; 发育异常  
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环境中逐年增加的工业化学品的生产使用、农药残留、药物滥用、空气污染、有毒有害食品等对人体健康的影响受到广泛关注。胚胎和胎儿对环境因素的危害更加敏感, 大量研究表明, 出生缺陷、不孕不育、生殖相关肿瘤等疾病与环境暴露之间存在着紧密的关联<sup>[1]</sup>。各类化学物质对胚胎或胎儿发育的潜在不良影响, 是人类与野生动物健康风险评估中必须考虑的一个重要因素。

发育毒理学研究数据通常来自妊娠实验动物在胚胎发育关键期暴露于不同浓度化合物的实验研究。为了比较来自不同国家和实验室的研究数据, 用于描述胚胎形态异常的术语与诊断标准必须统一。长期以来, 国际上未能对化学物质导致的各种胚胎形态异常和出生缺陷进行统一、标准化的归类, 这直接影响到化学物的健康风险评估和卫生监督政策。一种化学物质在一个国家可能被列为致畸物, 而在另一个国家则列为非致畸物。采用统一的术语与诊断标准, 可以使不同机构的科学家对发育毒性研究结果的解释更为一致, 并且使欧洲、美国和亚洲各国根据各自法规所进行的对于农药、杀虫剂和其他化学物质的风险评估、分类及标签更为透明。

为了推进上述研究的深入, 早在1995年, 国际畸形学学会联合会(International Federation of Teratology Society, IFTS)就开始从常用实验动物入手, 研究胚胎发育异常图像数据库, 用以呈现实验动物胚胎(新生幼仔)畸形和变异的图片、说明、分类和规范术语<sup>[2-4]</sup>。IFTS组织来自欧洲、北美洲和日本的相关科研机构参加了数据库的合作研究和编写。由德国联邦风险评估研究所牵头, 德国Charite大学医学院(原柏林自由大学临床药理

学和毒理学研究所)、WHO国际化学品安全规划署、美国环境保护署(Environmental Protection Agency, EPA)、英国中央毒理学实验室、日本京都大学共同参与, 耗时十余年, 编写了常用实验动物外观、骨骼及内脏形态异常解剖图像数据库。该图像数据库配有数千张详细的图片、描述、术语和统一分类, 极大地促进了发育毒理学研究中形态异常描述术语的统一和规范化。1999年完成第1版的《大鼠外观及骨骼形态异常解剖图像数据库》、《小鼠外观及骨骼形态异常解剖图像数据库》和《兔外观及骨骼形态异常解剖图像数据库》, 以CD-ROM光盘形式出版, 正式宣告了实验动物胚胎发育异常图像数据库(DevTox数据库)国际化合作网络的建设和启动<sup>[5]</sup>。

之后, IFTS每隔2-3年在德国柏林召开一次“实验动物胚胎发育形态异常术语和分类规范化研讨会”, 邀请来自各个国家的政府监管部门、研究院所、大学和企业的国际专家参会, 讨论实验室研究结果的更新, 增加包括母胎观察和非常用动物物种的最新研究结果、改善术语分类、更新图像数据库的版本等<sup>[6]</sup>。借此, DevTox数据库国际化合作网络的建设得以持续推进。迄今为止DevTox数据库已完成了第3版的更新出版工作。新版本的DevTox数据库在原有基础上增加了上千张形态异常的图片 and 说明, 对描述实验动物形态异常术语进行了规范化统一分类, 涵盖的动物种属也由之前的小鼠、大鼠和兔扩大至豚鼠、猪和灵长类动物。

为了使DevTox数据库能够更公开、更广泛、更便捷地与各国科学家所用, 数据库发表的形式也由CD-ROM光盘调整为网络免费共享平台(网址为[http://www.devtox.org/index\\_01\\_01\\_01.htm](http://www.devtox.org/index_01_01_01.htm))。

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DevTox introduction article in "Chinese Journal of Carcinogenesis, Teratogenesis, Mutagenesis"

# Chinese version of the DevTox data base

- The Chinese version of the DevTox Data Base was launched on the website in the end of 2016.
- Funding support of Federal Institute for Risk Assessment (BfR) and Shanghai Science and Technology Committee (STCSM)
- Technical support of BfR, Fraunhofer Institute for Toxicology and Experimental Medicine ITEM, CHARITÉ-Academical Medicine Berlin, Shanghai Institute of Planned Parenthood Research (SIPPR) and Fudan University.
- The translation covers all through the DevTox background information to the individual image descriptions, and has been revised many times to ensure its correctness and accuracy.

# Start DevTox: [www.devtox.org](http://www.devtox.org)

## DevTox

www.DevTox.org

A Resource for Developmental Toxicology



### .Background

The DevTox project  
Berlin workshops  
Project partners

Technical information

### .Nomenclature

### .Data

### .Masthead

中文



## Welcome

You have reached the relaunched Web site of the **DevTox Project** (Version 3.0).

This Web site is intended to provide a valuable resource for health professionals and researchers working in the field of developmental toxicology and represents one of the most comprehensive sources of images of developmental abnormalities.

There are three areas accessible on this site from the menus above, reflecting the main parts of the project:

#### ▶ **DevTox .Background**

Supplementary information on the **project** itself, the publications of the **DevTox Project** and the **Berlin workshops**, a list of **project partners** and relevant **links**.

#### ▶ **DevTox .Nomenclature**

The updated **harmonized nomenclature** for developmental toxicology, based on the revised IFTS terminology (**Makris et al. 2009**): More than **2,500 images** show examples for **external**, **skeletal**, **soft tissue** and **maternal-fetal** anomalies [last update October 2012]. The harmonized categorization achieved at the eighth Berlin Workshop has been included [update October 2016].

#### ▶ **DevTox .Data**

An electronic **data base** is under development, in which experimental data from developmental studies in rats and rabbits in different labs can be evaluated to develop a historical control data base in various strains of common laboratory animals.

The **DevTox** Project was initiated by the German Federal Ministry of Food, Agriculture and Consumer Protection (BMELV) and the Federal Ministry of the Environment, Nature Conservation and Nuclear Safety (BMU) under the auspices of the International Programme on Chemical Safety (IPCS).

In order to make ongoing improvements to this Web site, your comments and suggestions are most welcome. Please direct your comments to the **DevTox** Project co-ordinator at [DevTox@bfr.bund.de](mailto:DevTox@bfr.bund.de). If you would like to contribute images, **please click here**.



Last update: 17-Oct-2016 | Contact: [DevTox@bfr.bund.de](mailto:DevTox@bfr.bund.de)



From Dr Ruppert Kellner's  
ppt

# Chinese Version available since Oct. 2016 [www.devtox.org/index\\_zh.php](http://www.devtox.org/index_zh.php)

## DevTox

www.DevTox.org

发育毒理学资源之一



背景

术语集

数据

发行机构

English

DevTox项目  
柏林研讨会  
项目合作单位

技术信息

## 欢迎

您已进入全新推出的DevTox项目(3.0版)的网站。

本网站旨在为工作在发育毒理学领域的卫生专业人员与研究人员提供宝贵资源,是最全面的发育形态异常图片来源之一。

从上面菜单可分三个区域进入本网站,这也是本项目的三个组成部分:

### ▶ DevTox .背景

关于本项目的补充信息, DevTox项目与柏林研讨会的出版物,项目合作单位与相关链接列表。

### ▶ DevTox .术语集

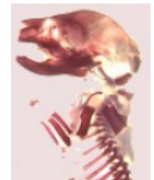
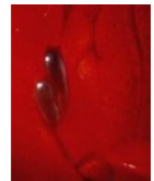
基于修订版IFTS术语集(Makris等2009)更新了发育毒理学统一术语集:2,500多幅图片展示了外观、骨骼、软组织以及母胎形态异常的各种图例。本网页也包括了第八届柏林研讨会上确认的统一分类[更新于2016年10月]。

### ▶ DevTox .数据

电子数据库正在开发中。通过该数据库可评估不同实验室的大鼠和兔发育学研究的实验数据,用以开发各品系常用实验动物的历史对照数据库。

DevTox项目由德国联邦食品与农业部(BMEL)以及联邦环境、自然保护与核安全部(BMU)发起,国际化学品安全规划署(IPCS)主办。

为不断改进本网站,热忱欢迎您的宝贵意见和建议。请将您的意见和建议直接提交DevTox项目协调处DevTox@bfr.bund.de。如您愿意贡献图片,请点击[这里](#)。





Head / Neck - Exencephaly

External finding

Synonym(s) -

Non-preferred term(s): Acrania

Definition:

Brain protrudes outside the skull due to absence of all or part of the cranial vault

Notes:

Erosion of brain

头/颈 - 露脑畸形

Head / Neck - Exencephaly

同义词:-

非首选术语: 无颅

定义:

由于颅骨全部或部分缺失, 脑突出到颅骨外

注释:

不像无脑畸形那样发生脑组织侵蚀

Fig. 12:

Additional finding: Open eye, macroglossia



Control

对照



大鼠, :对照图片

图片 12:

其他发现: 张眼, 巨舌



图片 13:

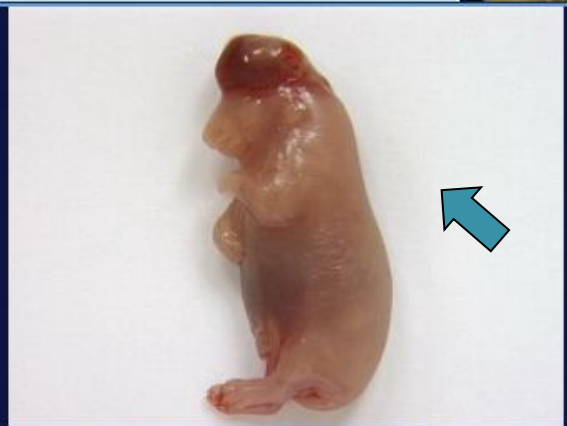
其他发现: 全身水肿, 短口鼻, 张眼(左)



图片 14:-



图片 15:-



图片 14: 大鼠, 头/颈 - 露脑畸形.



## DevTox. Background: Project partners

The following organizations have been involved in the development of DevTox:

- ▶ **Federal Institute for Risk Assessment (BfR)**  
Department 6: Chemicals Safety  
Max-Dohrn-Straße 8-10  
10589 Berlin  
Germany
- ▶ **Fraunhofer Institute for Toxicology and Experimental Medicine ITEM**  
Nikolai-Fuchs-Str. 1  
30625 Hannover  
Germany
- ▶ **Institute of Clinical Pharmacology and Toxicology**  
Department of Toxicology  
CHARITÉ – Academic Medicine Berlin  
Campus Charité Mitte  
Charitéplatz 1  
10117 Berlin  
Germany
- ▶ In addition, the valuable contribution of many prominent international scientists from research institutions, regulatory agencies, and industry is gratefully acknowledged.

## DevTox. 背景: 项目合作单位

以下机构参与了 DevTox 项目的开发与实施:

- ▶ **联邦风险评估研究所(BfR)**  
第六部: 农药安全性  
Max-Dohrn-Strasse 8-10  
10589  
德国柏林
- ▶ **Fraunhofer 毒理学与实验医学研究所(ITEM)**  
Nikolai-Fuchs-Str. 1  
30625  
德国汉诺威
- ▶ **CHARITÉ 大学柏林医学临床药理学与毒理学研究所毒理学研究室**  
Campus Charite Mitte  
Chariteplatz 1  
10117  
德国柏林
- ▶ **上海市计划生育科学研究所 世界卫生组织人类生殖研究合作中心 复旦大学**



## Chinese version of DevTox


- DevTox website represents one of the most comprehensive sources of images of developmental abnormalities.
- The purpose of launching Chinese version of DevTox is to introduce this valuable resource to Chinese health professionals and to promote the terminology harmonization of the developmental abnormalities.
- Call for Chinese researchers to share good images of developmental abnormalities with DevTox and international scientific community.

## 2. Pictures uploaded to the Data Base

- Besides the translation work, we also worked on teratogenic tests and submitted new images to the DevTox Data Base.
- Until now 25 images of rat visceral anomalies and 20 images of mouse visceral anomalies have been uploaded to the Data Base.







**An image analysis of external  
and skeletal malformation  
induced by retinoic acid (RA) in  
SD rats**

## Teratogenic tests

- Teratogenic tests are used to assess the effects of chemicals on the development of pregnant animals, embryos and fetuses.
- Reproductive toxicity tests of drugs, cosmetics and pesticides are essential.

## Positive Control

- It is important to select positive controls with high teratogenic rate, low mortality, stable phenotype and good repeatability to ensure the authenticity and reliability of the teratogenic test.
- Vitamin A, acetaminophen, cyclophosphamide, aspirin, diethylstilbestrol and retinoic acid (RA)

## Retinoic Acid

- Retinoic acid is the active metabolite of vitamin A and plays an important role in the development of vertebrate embryos.
- Retinoic acid affects neurogenesis, cardiogenesis, body axial extension, kidney and eye development. Excessive exposure to retinoic acid can lead to abnormal embryonic development and multiple organ deformities.

# Method

40 pregnant rat  
GD10;  
Administered via  
gavage with RA at  
doses of 50, 100, 150  
 $\text{mg}\cdot\text{kg}^{-1}$  or corn oil.

at GD20, embryo  
implantation and  
development were  
observed;  
External anomalies  
observed.

embryos were stained  
by alizarin red;  
Skeletal anomalies  
observed.

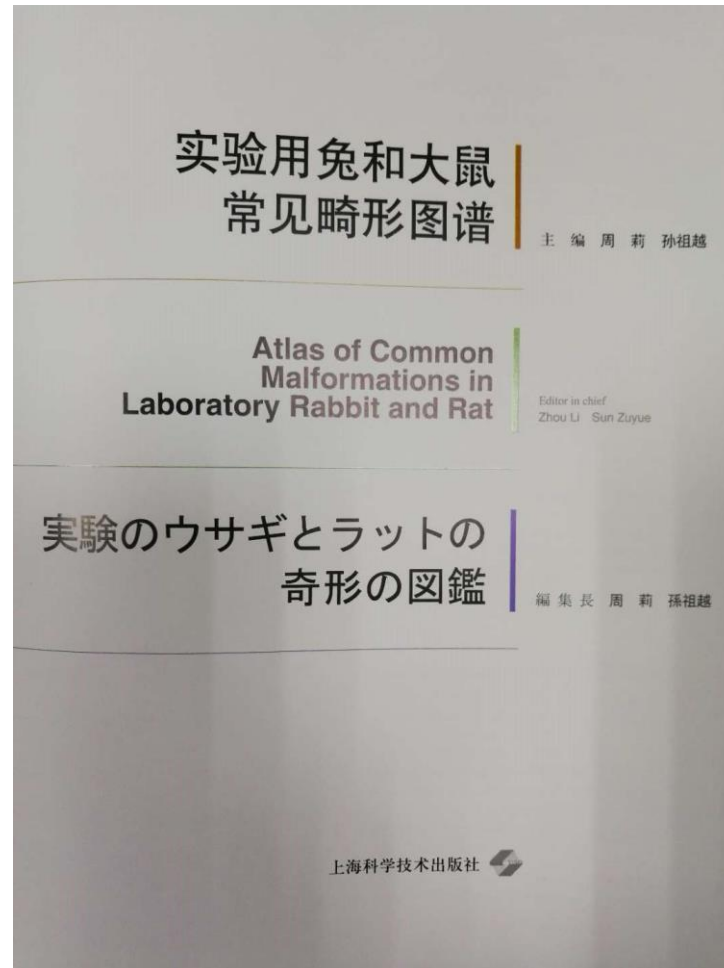
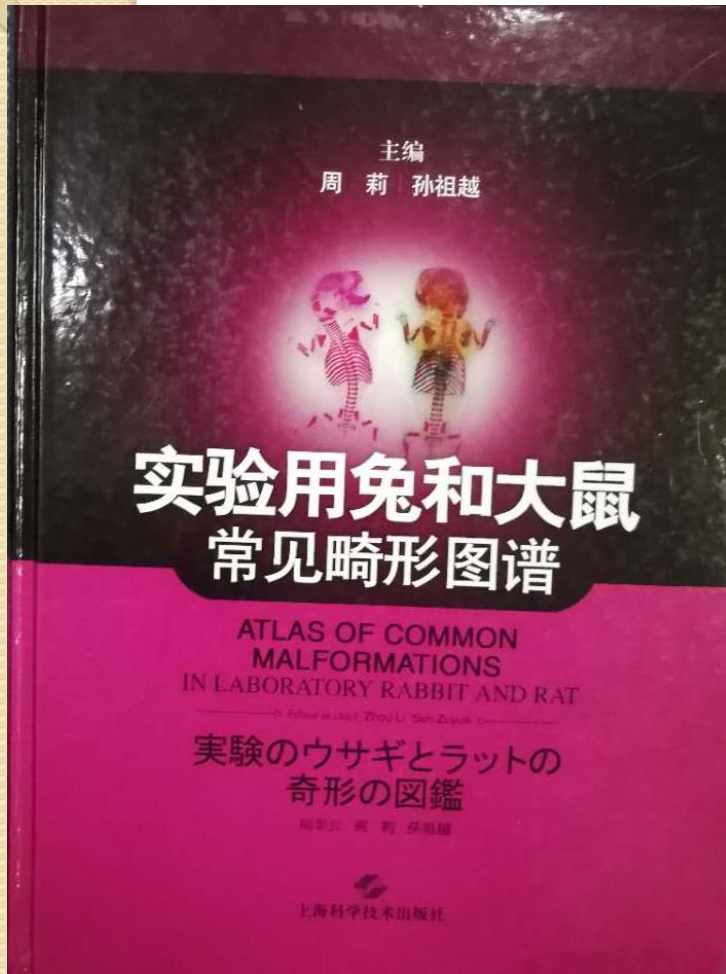
# The incidence of anomalies of the embryos induced by RA


**Table 2 The incidence of abnormalities of the embryos induced by different doses of RA**

Teratogenic types	control	RA 50mg/kg (%)	RA 100mg/kg (%)	RA 150mg/kg (%)
Lower jaw absent	0	100	100	100
Eye protruding	0	100	100	100
Pinna small	0	100	100	100
Small	0	100	100	100
Tail absent	0	100	100	100
Paw malrotated	0	100	100	100
Spina bifida,	0	34.62	100	100
Symmelia	0	2.56	17.65	0
Umbilicus projection	0	1.28	9.30	0
Unilateral eye absent	0	0	2.33	0
Generalized edema	0	0	20.93	50



# 5. Atlas of common malformations in Laboratory Rabbit and Rat, SIPPR, China



- 
- Chinese book of *Atlas of Common Malformations in Laboratory Rabbit and Rat* has been published recently, which contained more than 500 original abnormality images.
  - If these images could be shared with DevTox, the data base resource would be further enriched.

# Rabbit anomalies



Meningo-encephalocele (dorsal view)



Palpebral absent (lateral view)



Thorco-gastroschisis (lateral view)



Syndactyly, claw absent (lateral view)

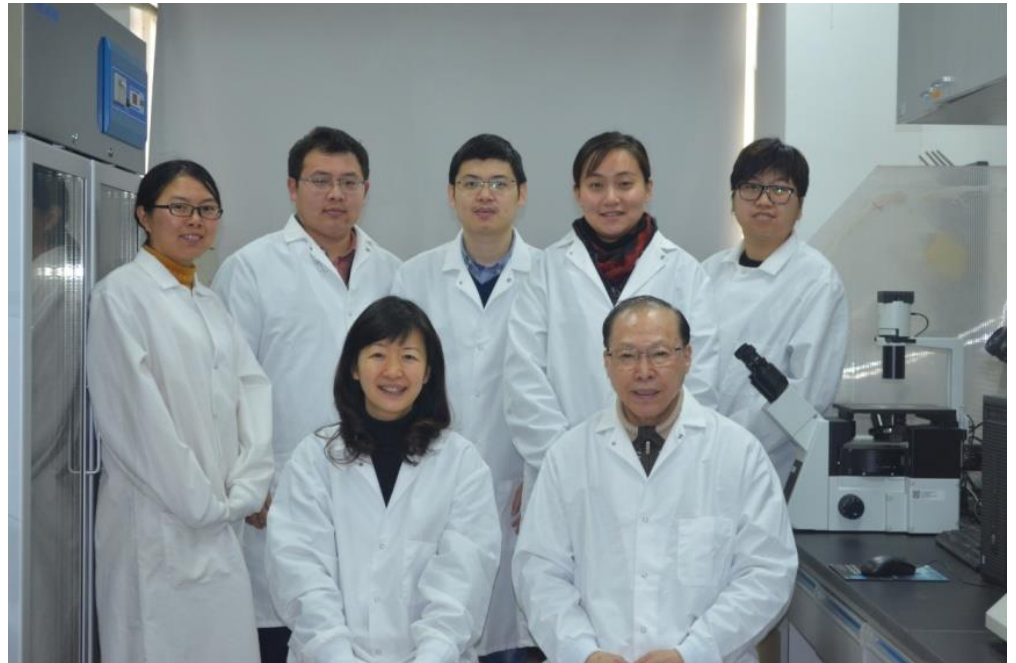


Hyperflexion (ventral view)



# Thank You

BfR  
Fraunhofer ITEM  
CHARITÉ- Academic Medicine Berlin  
SIPPR  
Fudan University



Colleagues from SIPPR