
UPDATE OF NEW IMAGES AND CATEGORISATION IN THE *DEVTOX* DATABASE

Rupert Kellner



OVERVIEW

- New images in *DevTox*
- Categorisation of anomalies
- Translation of *DevTox*

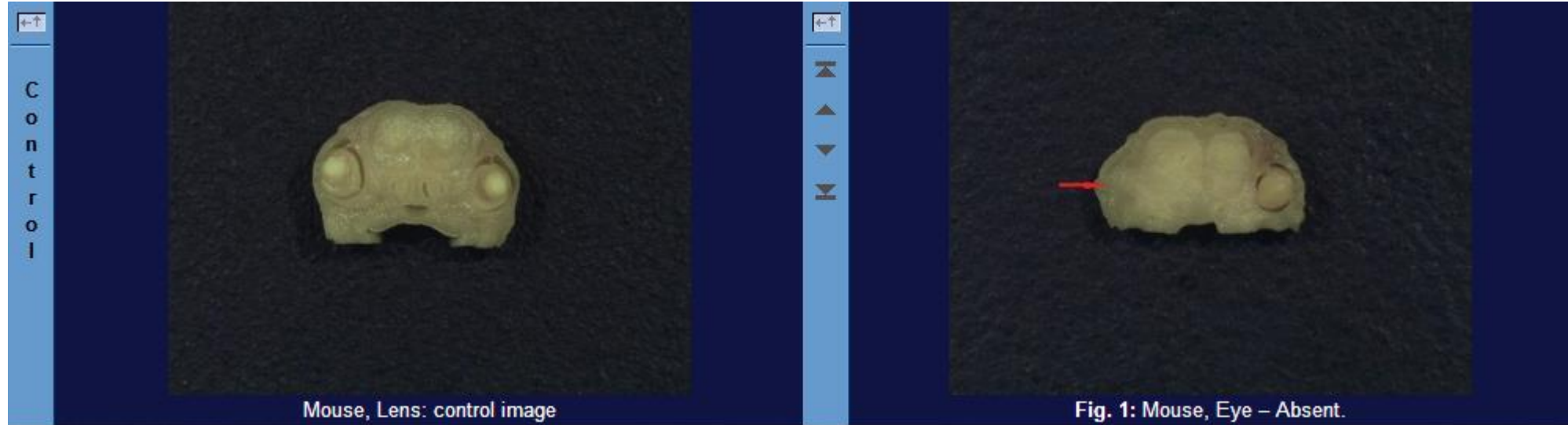
New Images in *DevTox*

- Visceral anomalies
 - Images supplied by Dr. Jingying Hu, Shanghai
 - Selected to represent hitherto unillustrated anomalies
 - 33 new images on anomalies and additional control images

- Result: Total of 212 images on visceral anomalies

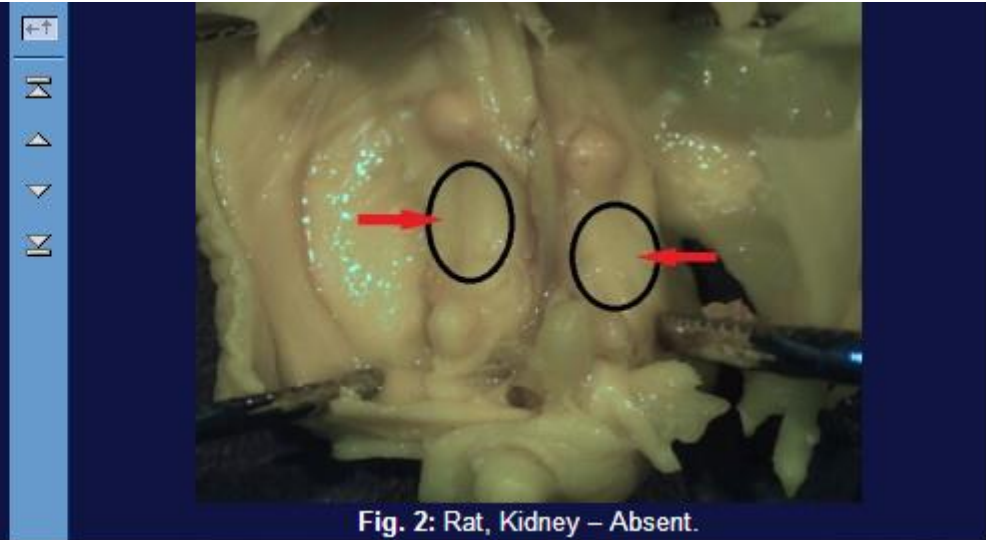
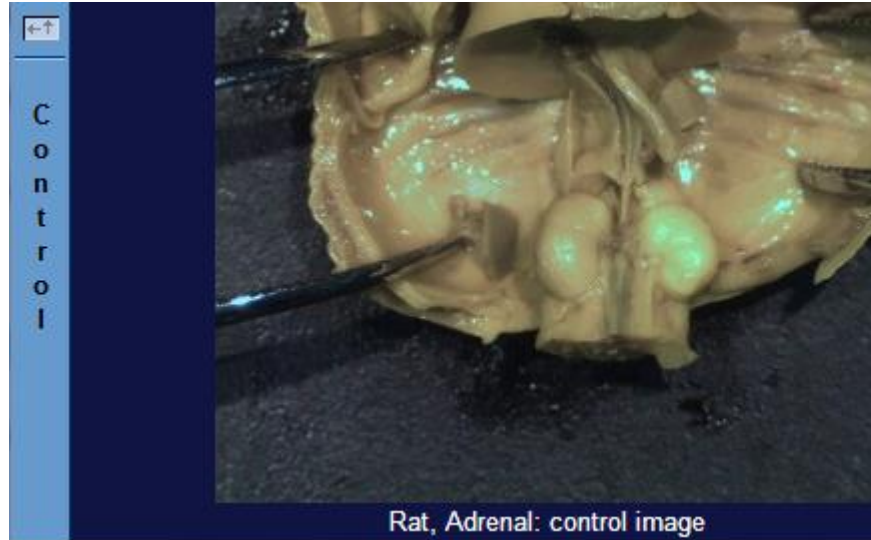
Examples for New Images

- Eye – Absent
 - First example in the mouse



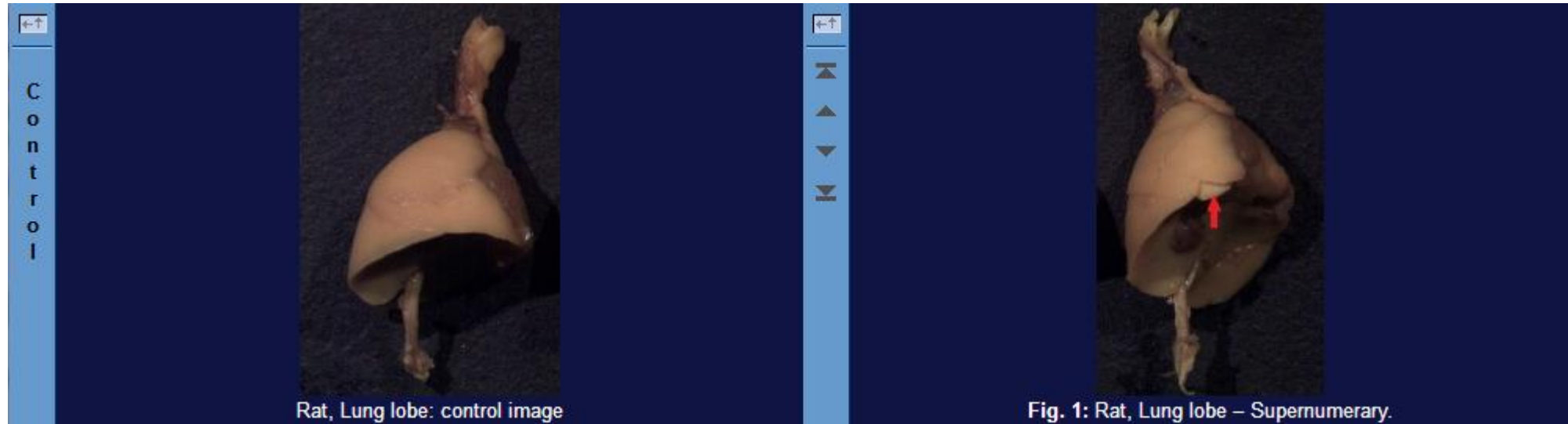
Examples for New Images

- Kidney – Absent
 - First three examples in the rat (see one below)
 - First example in the mouse



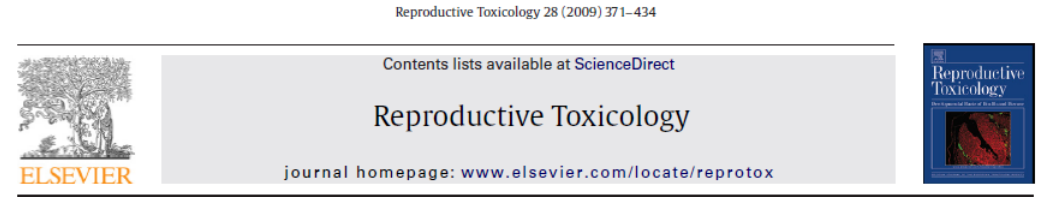
Examples for New Images

- Lung lobe – Supernumerary
 - First example in any species (rat)



Categorisation of anomalies

- Terminology of developmental anomalies (version 2)
- According to Makris et al. 2009
- Categorisation in previous terms preserved
 - Malformation ■ M
 - Grey zone anomalies ■ G
 - Variation ■ V
- Many terms “not classified”



Terminology of developmental abnormalities in common laboratory mammals (version 2)^{☆,☆☆}

Susan L. Makris^{a,*,1,4}, Howard M. Solomon^{b,1,4}, Ruth Clark^{c,2,4}, Kohei Shiota^{d,3,4},
Stephane Barbellion^{e,2}, Jochen Buschmann^{f,2}, Makoto Ema^{g,3}, Michio Fujiwara^{h,3},
Konstanze Grote^{i,2}, Keith P. Hazelden^{j,1}, Kok Wah Hew^{k,1}, Masao Horimoto^{l,3},
Yojiro Ooshima^{m,3}, Meg Parkinson^{n,2}, L. David Wise^{o,1}

Example from *DevTox*

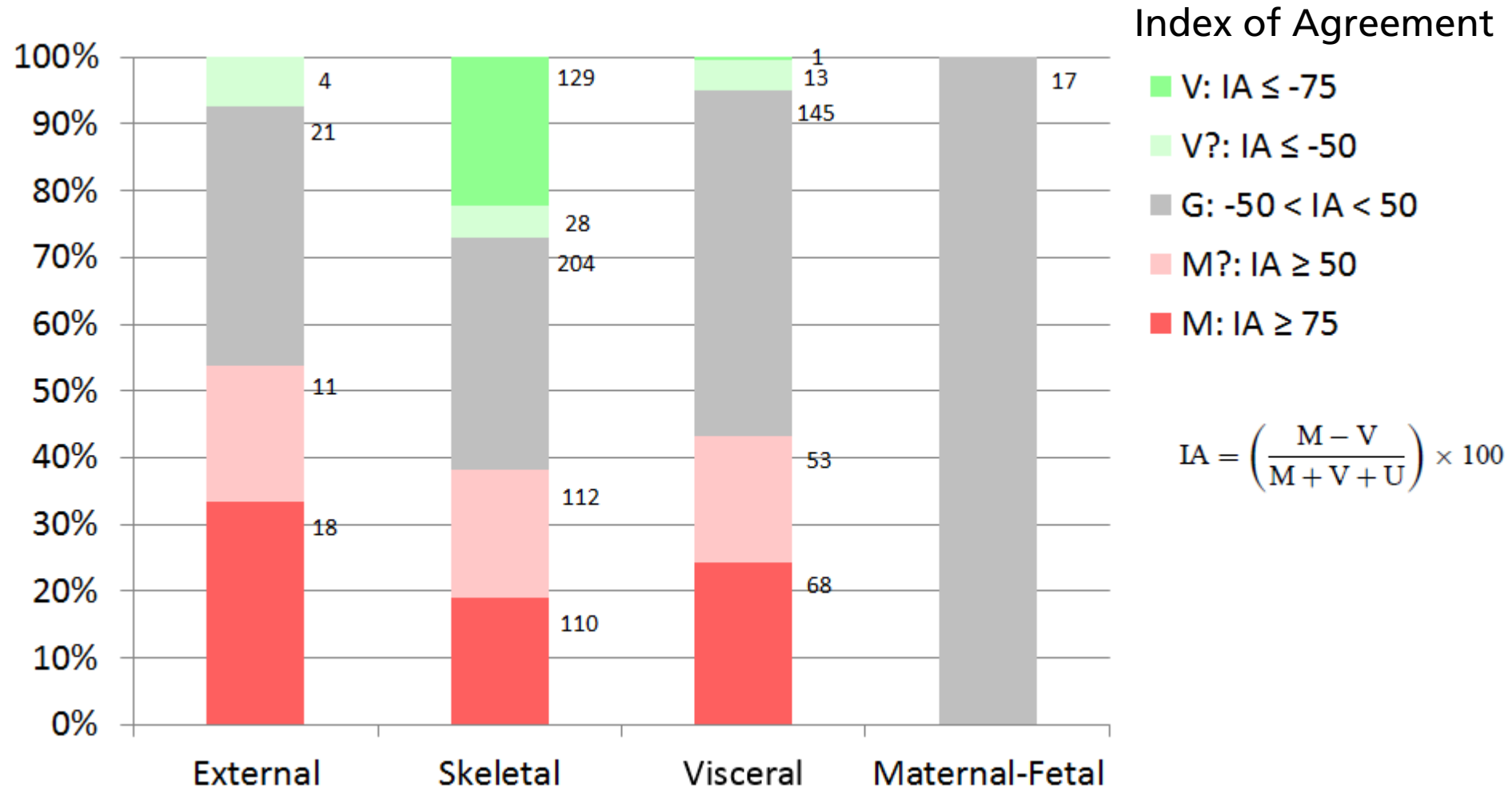
Skeletal Findings: Mandible [Status of 2012]

Mandible	①	②	③	④	⑤	⑥	⑦	⑧	⑨
Absent	—	—	—	—	—	—	—	—	—
Bent	—	—	—	—	—	—	—	—	—
Fused	—	—	—	✓	—	—	—	—	—
Hole	—	—	—	—	—	—	—	—	—
Incomplete ossification	✓	—	—	—	—	—	—	—	—
Increased ossification	—	—	—	—	—	—	—	—	—
Isolated ossification site	—	—	—	—	—	—	—	—	—
Large	—	—	—	—	—	—	—	—	—
Long	—	—	—	—	—	—	—	—	—
Malpositioned	—	—	—	—	—	—	—	—	—
Misaligned	—	—	—	—	—	—	—	—	—
Misshapen	—	—	✓	—	—	—	—	—	—
Short	✓	—	—	—	✓	—	—	—	✓
Single incisor socket	—	—	—	—	—	—	—	—	—
Small	✓	—	✓	—	—	—	—	—	—
Splayed	—	—	—	—	—	—	—	—	—
Supernumerary	—	—	—	—	—	—	—	—	—
Supernumerary site	—	—	—	—	—	—	—	—	—
Thick	—	—	—	—	—	—	—	—	—
Thin	—	—	—	—	—	—	—	—	—
Unossified	—	—	—	—	—	—	—	—	—
Unossified area	—	—	—	—	—	—	—	—	—

Symbols:
 ①: Rat (Ra)
 ②: Mouse (Mo)
 ③: Rabbit (Rb)
 ④: Hamster (Ha)
 ⑤: Primate (Pr)
 ⑥: Guinea Pig (Gp)
 ⑦: Minipig (Mp)
 ⑧: Dog (Do)
 ⑨: Bird (Bi)
 — : absent in species
 — (red) : malformation
 — (grey) : present
 — (green) : variation
 — (light grey) : not classified
 ✓ : image(s) available
 P : post-natal image(s) available

- Survey in 2013 to fill the gaps
 - External: 54
 - Skeletal: 567
 - Visceral: 273
 - Maternal-Fetal: 17
- 20 questionnaires from experts / expert groups

Result of the Survey in 2013



Implementation of the Categorisation in *DevTox*

- Most classifications added according to the Survey: 932 anomalies
- Slight modifications of the results of the Survey
 - Discussion at 8th Berlin Workshop in 2014
 - Visceral anomalies:
 - Posterior (caudal) vena cava - Branching variation
 - Subclavian artery - Branching variation

Subclavian artery	①	②	③	④	⑤	⑥	⑦	⑧	⑨
Absent			✓						
Branching variation									
Dilated									
Malpositioned									
Narrow									
Retroesophageal		✓	✓						
Supernumerary									
Supernumerary branch									

Symbols:

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- : absent in species
- : malformation
- : grey zone
- : variation
- ✓ : image(s) available
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Example from *DevTox*

Skeletal Findings: Mandible [Current Status]

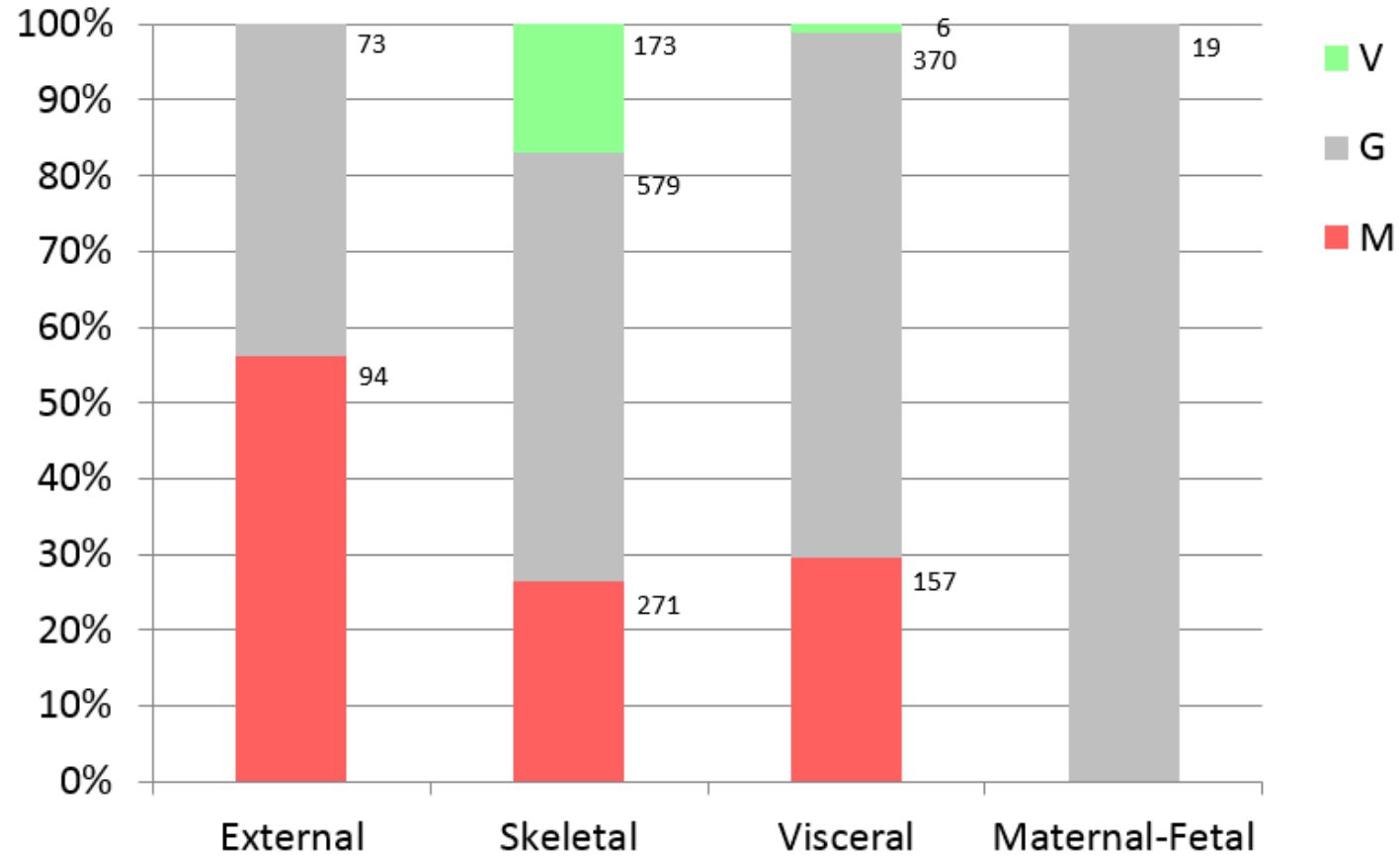
Mandible	①	②	③	④	⑤	⑥	⑦	⑧	⑨
Absent									
Bent									
Fused				✓					
Hole									
Incomplete ossification	✓								
Increased ossification									
Isolated ossification site									
Large									
Long									
Malpositioned									
Misaligned									
Misshapen			✓						
Short	✓			✓					✓
Single incisor socket									
Small	✓	✓							
Splayed									
Supernumerary									
Supernumerary site									
Thick									
Thin									
Unossified									
Unossified area									

Symbols:

- ①: Rat (Ra)
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- ⑨: Bird (Bi)
- : absent in species
- (red): malformation
- (grey): grey zone
- (green): variation
- ✓: image(s) available
- P: post-natal image(s) available

Mandible	2012	①	②	③	④	⑤	⑥	⑦	⑧	⑨
Absent										
Bent										
Fused					✓					
Hole										
Incomplete ossification	✓									
Increased ossification										
Isolated ossification site										
Large										
Long										
Malpositioned										
Misaligned										
Misshapen			✓							
Short	✓				✓					✓
Single incisor socket										
Small	✓	✓								
Splayed										
Supernumerary										
Supernumerary site										
Thick										
Thin										
Unossified										
Unossified area										

Summary of Current Categorisations in *DevTox*



Translation of *DevTox*

Translation into Chinese version

- Proposed at the 8th Berlin Workshop in 2014
- Preparation of templates in autumn 2014
- Translation in China (Dr. Weihua Li)
 - Shanghai Institute of Planned Parenthood Research
 - WHO Collaboration Centre for Research in Human Reproduction
 - Fudan University
- Translated files in several lots from summer 2015 to spring 2016
- Implementation in the website
- Final checks at BfR (Dr. Wenna Xu)
- Release to the public in autumn 2016



Reduction of the Variety of Text Sources

Original English version

- Text files (HTML)
- PHP program scripts (Server)
 - Access database and arrange pages
- Database tables
- JavaScript programs (Browser)
 - Build e.g. menus
- Button icons with info



Modified English version

- Text files (PHP)
- Database tables

Programs are still active but do not contain any text information displayed on screen

Example DevTox General Pages: Background

DevTox A Resource for Developmental Toxicology www.DevTox.org

DevTox .Nom background **DevTox** 发育毒理学资源之一

As a result of the Berlin Workshops, the "DevTox database" was promoting harmonization and standardization of nomenclature classification and labeling of hazardous chemicals.

The use of a harmonized and internationally accepted nomenclature terminology is used in all studies, a comparison of data across terminologies was made in 1997 by a publication of the International Commission on Occupational Health (ICOH) and the Federal Institute for Risk Assessment (BfR) and the Free University of Berlin. The **Toxicology** took place since then in Berlin with the goal to eliminate definitions for the two classification categories "malformation" and "adverse effect".

The results of all these activities were used to establish the **lexicon** made by clearly dividing a diagnosis into a **localization** term and an observation term. Furthermore, a hierarchical structure for the classification was established.

From the information stored in the lexicon of the **DevTox data Nomenclature information system**, called "**DevTox.nom**", images and data and a quick navigation throughout the complete external, skeletal, soft tissue and maternal-fetal anomalies in rat.

New topics covered by the system are specific aspects in relation to the following areas. For a better understanding of these specific aspects, see:

- [topography of the avian skeleton](#)
- [images on postnatal normogenesis of the rodent skeleton](#)

In addition, the Web site provides short descriptions of each finding to contribute to this site by [submitting additional images](#).

Most images were contributed by Brigitte Woelffel. The images of postnatal anomalies in the rat were taken by the induzierten Effekten durch die klassische teratogene Substanz 5-Fluorodesoxyuridin (FDUR) bei Ratten."

The supervisor of both is Prof. Dr. Ibrahim Chahoud, Institute of Occupational and Environmental Health, Free University of Berlin.

After successful completion of the update, the Web site was reloaded. A total of 1742 observations is available, of which 911 were introduced into the database. Based on the new images, a list of findings still not yet classified is available.

DevTox .术语集 背景 数据 发行机构 English

"DevTox数据库"的建立证明了这促进了术语与描述性词汇的统一和标准化,而且该数据库作为研究工具,对危险化学品的分类与标识非常有用。

使用统一和国际公认的术语是DevTox应用这类数据库的基本要求。只有所有研究都使用相同术语,才有可能对不同实验的数据进行比较。1997年畸形学学会国际联合会IFTS的出版物(Teratology, 55, 249-292, 1997)最早编纂了这种统一术语集。随后,由(德国)联邦风险评估研究所(BfR)和柏林自由大学于1995年发起的**发育毒理学学术语系列研讨会**在柏林应运而生,目的是消除IFTS术语内模糊不清与矛盾之处,并为"畸形"与"变异"两个分类类别确定工作定义。

利用以上所有工作的成果建立了**DevTox数据库的**词库。为了更好地应用于计算机系统,将诊断明确区分为**解剖学定位术语**与**观察结果术语**,并从观察结果术语中去除了所有解剖学部位的描述。此外,还增加了解剖学定位的层级结构。

由存储在**DevTox数据库**词库中的信息以及项目合作单位提供的图片与数据,创建了名为"**DevTox.nom**"的网络**DevTox术语信息系统**。易于使用的Web界面使用户可以从术语、图片与数据等不同视角,在整个网站内快速航行。**DevTox.nom**内目前有2,500多幅图片,展现了大鼠、小鼠、兔、仓鼠、灵长类动物、豚鼠、小型猪、狗与鸟的外观、骨骼、软组织以及母-胎畸形的各种例子。

本系统包含的新专题是关于**鸟类骨骼**和哺乳动物骨骼系统**出生后发育**的具体问题。为更好理解这些具体问题,请参阅:

- [鸟类骨骼局部解剖学](#)
- [啮齿类动物出生后骨骼的正常发育图片](#)

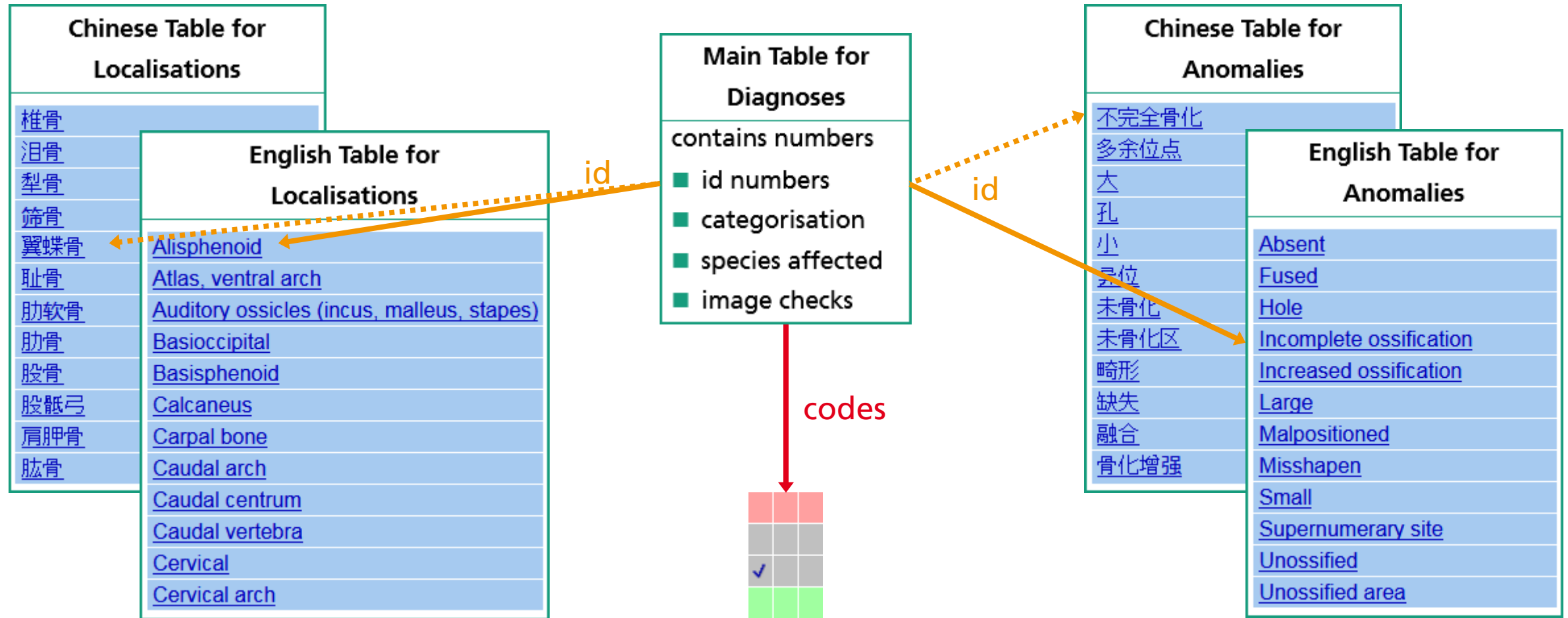
此外,本网站提供了每项观察结果的简要介绍,其中一部分还有同义词以及进一步的诊断说明。本网站诚邀所有用户积极**提交更多图片**,以促进网站发展。

大部分图片由Brigitte Woelffel女士提供。大鼠出生后畸形图片由当时的博士研究生Alice Walter女士拍摄。其论文题目是:"Untersuchung von pränatal induzierten Effekten durch die klassische teratogene Substanz 5-fluoro-desoxyuridine (FDUR) auf das Skelettsystem hinsichtlich ihrer postnatalen Persistenz bei Ratten." 她们两人的导师均为柏林Charité临床药理学与毒理学研究所教授Ibrahim Chahoud(博士)教授。

本网站成功完成更新后,于2012年10月被重新推出,为围绕新的研究结果进行科学讨论提供基础。网站上有1742项研究结果,其中引入911项,重命名831项,【删除了66项旧结果】。数据库中新增691幅图片。在这些新图片的基础上,编撰了一份尚未被新术语集所收录的研究结果列表。确定了一些重要发现,并将展示实例。这些新术语尚未得到畸形或变异的归类。该术语集收录了新引入动物种属的绝大多数研究结果,但有些解剖结构(如叉骨、腕掌骨及跗跖骨等)被确定为某些新物种特有的。

新术语集涵盖了本网站许多新的研究结果,且能够反映新品种中大多数畸形以及动物出生后观察到的许多发育早期畸形。下次更新时将考虑尚未被收录到术语集内的新物种研究结果,并应以灵长类动物中的研究结果为重点。之后,应将新的研究结果分类为畸形、变异或处于"灰色地带"的畸形。

Internal Structure of the Database



Home Index Locations Findings Manuscript Comments ? DevTox Ra Mo Rb Ha Pr Gp Mp Do Bi

Rib – Fused Skeletal finding M

Synonym(s): Cartilaginous fusion
 Non-preferred term(s): –
 Definition:
 Joined or blended together

Fig. 7: 7 day p.n.
 Rib fused
 Additional finding: Thoracic centrum Bipartite ossification, Fused, Malpositioned



Example Rib – Fused

主页 解剖学定位 结果 文本 评论 ? DevTox Ra Mo Rb Ha Pr Gp Mp Do Bi

肋骨 – 融合 骨骼结果 M

Rib – Fused

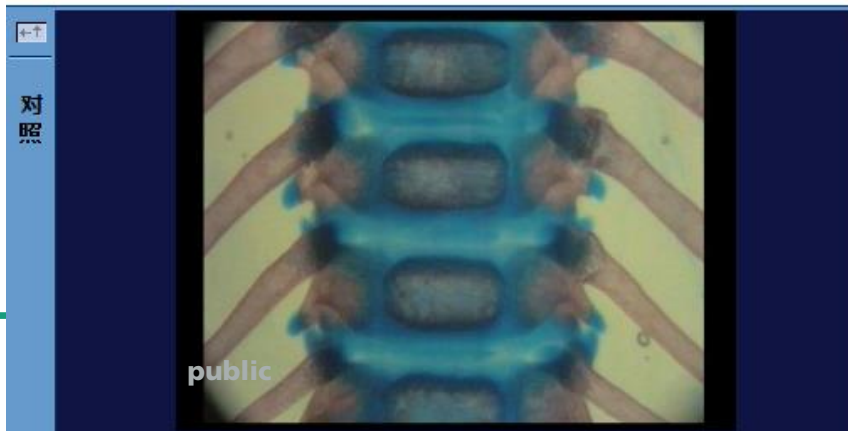
同义词: 软骨融合
 非首选术语: –
 定义:
 连接或融合在一起
 注释:
 详细说明融合的结构

图片 5:
 其他发现: 第13胸椎腹侧骨化中心双位点骨化, 额外第14肋骨

图片 6: –

图片 7: 妊娠第7天
 肋骨融合
 其他发现: 胸椎体双位点骨化, 融合, 异位



大鼠, 肋骨: 对照图片



图片 7: 大鼠, 肋骨 – 融合.

Conclusions About the *DevTox* Translation

- Structural rearrangements behind the scenes
 - Texts separated into a few files and the database tables (one devoted to global character strings)
 - Switch to different character set (UTF-8)
 - Programs modified to include the new resources
- [Translation of all texts]
- Implementation
 - Additional tables for new language
 - Programs for filling those new tables
 - Selection of additional language on the website
- Updates need to be considered