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Editorial Open Access

Importance of Databases for Human Genetic Diagnostics

Thomas Liehr *

Institute of Human Genetics, Jena University Hospital, Friedrich Schiller University, Jena, Germany

***Corresponding author:** Thomas Liehr, Institute of Human Genetics, Jena University Hospital, Friedrich Schiller University, Postfach, D-07740 Jena, Germany, Tel: +4936419396850; Fax: +4936419396852; E-mail: Thomas.Liehr@med.uni-jena.de

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Editorial

As recently outlined elsewhere by us [1-3] and others [4-6], human genetic laboratory diagnostics needs well-educated specialists. A most comprehensive and informative diagnostics result for each individual patient is the primary goal of each diagnostic effort [4]–personalized medicine is here one "hot topic term" nowadays [7].

Accordingly, the identification of a genetic aberration and its exact characterization is not enough. It is (i) necessary to understand what kind of genetic aberration is present [1-3], (ii) the chromosomal rearrangement must be described exactly according to international standards [8], and (iii) it is duty of a diagnostic laboratory also to provide in the report information on previously reported comparable cases (as outlined here). Major drawbacks have been recently reported for (cyto) genetic expertise [2,9], choice of reliable methods [3,10,11] and overall the need for education of specialists working in human genetic diagnostics [12].

Here the reader's attention shall be focused on three databases, which may be of great help in case of reporting about constitutional pericentromeric chromosomal imbalances [13], constitutional Uniparental Disomy (UPD) [14] and constitutional cytogenetically visible copy number alterations [15]. Generally, free access to these three databases (and an additional one on mFISH - basics and literature on multicolor fluorescence *in situ* hybridization application [15], not covered here) can be achieved via http://ssmc-tl.com/Start.html.

The database on pericentromeric chromosomal imbalances (http://ssmc-tl.com/sSMC.html) provides a collection on >6,000 small supernumerary marker chromosome (sSMC) and ~100 other cases with centromere-near imbalances, reviewed from the literature and/or studied in my lab (~16% were studied in Jena, Germany). Also included are basic information on sSMC and the clinical impact of pericentromeric chromosomal imbalances. Interestingly, the latter are in many cases not leading to clinical problems, as there may be DNA-stretches of several mebabasepair in size, which do not contain any dosage sensitive genes [16]. These regions are speci ied in this database, which thus can be used for comparison and interpretation of own clinical cases. Submissions of further well characterized cases are welcome using the form available under http://ssmc-tl.com/case-submission.html#case.

In the second database (http://upd-tl.com/upd.html) >3,600 cases with uniparental disomy (UPD) are included. They are divided by chromosomal origin, paternal or maternal origin of the UPD, and such cases where the UPD was only detected by SNP-array or next generation sequencing in the index patient. This collection was a kind of 'spin-off' of the sSMC page, as UPD is also a problem in a subset of these patients. Interestingly, at least 30% of UPD cases evolved due to chromosomal aberrations [17]. This database can also be accessed via https://omictools.com/uniparental-disomy-tool.

Finally, a collection of >200 euchromatic and >200 heterochromatic copy number variant (CNV) regions without any clinical consequences was the 'second offspring' which developed from the sSMC database (http://upd-tl.com/HMs.html). Here cytogenetically visible CNVs, often confusing cytogenetic diagnostics, are included. In contrast to the first two databases, here not each reported case but only each reported variant is listed. It was a surprise that yet as many euchromatic as heterochromatic cytogenetically visible CNVs are known. For sure some overlap of the euchromatic cytogenetically visible CNVs with other databases exists, like Decipher (https://decipher.sanger.ac.uk/) or the Database of Genomic Variants (http://dgv.tcag.ca/).

With >5,500 accesses to these three pages in 2017 these databases are already well appreciated by the community. Nonetheless, maybe this editorial may guide some more potential users to these valuable tools in the next years.

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