Metabolomics - what nomenclature to use?

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Abstract – This Opinion paper was written to initiate a discussion on the nomenclature used in metabolomic studies. The paper is based on the belief that the currently used classification of metabolites as "primary" and "secondary" are inaccurate and somewhat misleading. Of the alternative names previously suggested in the literature we strongly support the use of the names "general" and "specific metabolites" as replacements of "primary" and "secondary", respectively.

Keywords – nomenclature, metabolomics, general metabolite, primary metabolite, specific metabolite, secondary metabolite

Discussion

What is metabolomics? A typical metabolomic study aims at analyzing as many metabolites as possible from a single biological sample. The technology already has different well-established analytical platforms that rapidly develop from semi-quantitative to absolute quantitation of the analytes.

The question arises: what nomenclature to use when interpreting data of metabolomic investigations? In our opinion, the nomenclature widely used today needs to be revised. This is the reason why we are writing this paper to initiate a discussion on this subject.

Today's metabolite classification was introduced in 1891 by Albrecht Kossel (Kossel, 1891) (later winner of the Nobel Prize in Medicine) who used the term “secondary” to separate less important metabolites from “essential” ones (those he named “primary”). In this way, the terms primary metabolism and secondary metabolism were also created.

The accuracy and well-foundedness of Kossel's classification (at least, for those he suggested as "secondary" metabolites) has been questioned on several grounds (Bennett and Bentley, 1989; Frank, 1998; Firn and Jones, 2009), and a number of alternative names were suggested (Table 1; the list is not meant to be comprehensive).
1. Table. Alternative names suggested for Kossel's "secondary" metabolites.

| Name                                           | Reference |
|------------------------------------------------|-----------|
| "Shunt" metabolites (i.e., waste products)     | (Foster, 1949) |
| Metabolite classes I, II and III                | (Gaden, 1959) |
| Natural products                                | (Zhang and Demain, 2005) |
| Idiolites                                       | (Walker, 1974) |
| Stress metabolites                              | (Haard, 1983) |
| Phytochemicals (plant chemicals)                | (Harborne, 1973) |
| Specific metabolites                            | (Bennett and Bentley, 1989; Frank, 1998) |
| Ecochemicals                                    | (Hartmann, 2007) |
| Specialized metabolites                         | (Chae et al., 2014) |

For us, from the above list the terms "specific" and "general" as opposed to "secondary" and "primary" metabolites seems to be the best, by far. "General" is accurate in the sense, that these metabolites can generally be found in all living cells of an organism. "Specific" is correct, because these metabolites are found in a way that is indeed specific in several aspects, such as taxa, cell, tissue, organ, developmental stage, presence or absence of nutrients and stress, etc. Further, detailed, scientifically well-founded support for this nomenclature can be read in two excellent papers: 1) in which it was first suggested (Bennett and Bentley, 1989), and 2) where the idea was first reviewed and a clear and precise definition for specific metabolites was given (Frank, 1998).

Conclusions

In the near future the technology of metabolomics will certainly lead to a number of new discoveries related to yet unknown metabolites. Regulatory routes of their synthesis will be characterized, new biological functions (and evolutionary benefits) and new human uses will be found, etc. Since the correctness of the nomenclature used in this rapidly expanding field is essential, we invite teachers, researchers, and scientists to express their opinion on this subject. General biology, evolutionary biology, functional biology, and metabolomics as a branch of science may all benefit from this discussion.

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Public interest statement

This Opinion paper is written to invite scientists for a discussion on the nomenclature to be used to describe and evaluate findings of metabolomic studies. We support the use of "specific metabolite" instead of the currently used "secondary metabolite" and also "general metabolite" instead of "primary metabolite".

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