‘Plasma Lipidomics: Reference Values’

26-27 November 2018
National University of Singapore

Main Goals

1) Reach a consensus regarding suitable workflows for harmonized plasma lipidomics, including lipid extraction methods, reference materials and calibrators to generate robust plasma lipidomics data and to identify a priority list of plasma lipids for which reference values should be developed
2) Decide on suitable target populations (i.e. paediatric, adult vs geriatric; ethnicities; gender; healthy vs populations at risk)
3) Chart a roadmap to achieve this goal (i.e. who, what, when and how; available resources and potential partners)

Background

This gathering builds on a successful workshop held in Singapore in April 2017, where an international group of experts discussed mass spectrometry-based lipidomics of human plasma, and available platforms for analysis and data sharing. This community-led initiative resulted in a position paper (Burla et al, JLR 2018) summarizing the various aspects of pre-analytical, analytical and post-analytical workflows involved in plasma lipidomics.

We now wish to move to the next phase and invite the community to come to a consensus regarding suitable workflows for harmonized plasma lipidomics. Ideally, in the future this will lead to a few 'locked-in' methods with respective reference materials and calibrators, which can then be universally applied to derive and report plasma lipidomics data.

We also propose to discuss the topic of biological variation of plasma lipids and its impact on generating and interpreting population reference values, considering individuality (inter- and intra-individual variations) as an important factor.

Details on main goals

1) Short list of plasma lipids for which reference values should be developed

In this session we wish to discuss potential lipid candidates for which the community could determine reference values. This decision could be driven by (i) availability of robust, standardized measurement protocols for that lipid and (ii) a biological or clinical utility for having this lipid's reference value. The outcome of this discussion would ideally be a list of plasma lipids of interest to the community, with their suggested measurement protocols ('reference method') as well as suitable reference materials to allow for metrological traceability, and a consensus on adequate data reporting. Additional topics might include suggested study design i.e. when and how often a particular lipid species should be measured, and potential lipid-specific preanalytical requirements (sample type and volume, collection vials, storage etc.).

The list of target analytes could include lipids for which no reference values have been determined yet, as well as lipids such as cholesterol esters and triacylglycerides, for which reference values exist for their total sum but not yet for individual molecular species.

2) Target populations

In this session we wish to discuss potential target populations for which we could establish reference values. The background of this topic is that most existing reference values were determined in a subgroup of the global population: male Caucasians aged 25-35 years. This discussion could be driven by an evaluation of the impact of having reference values for specific populations, i.e. which population would benefit the most from having specific reference values. For example, it is well accepted that existing reference values do not accurately represent children. Also, more and more evidences are emerging for ethnicity-based differences (or associations) for certain measurands.

This discussion could also extend to the topic of the differences between population-based reference values versus individual ones. An important aspect here will be the concept of individuality of measurands, i.e. the determination of the within- and the between-subject variation, and the consequences for interpretation of reference values. For background information on this concept, please refer to 'Biological Variation: From Principles to Practice' by Callum G Fraser (AACC Press).

3) Roadmap for next stages – major discussion items

- Decision on work packages: which lipid panel will be measured, in which populations, with which analytical workflows?
- Decision on working groups to address the above issues and estimated time frame
- Organization of experimental approach: usage of existing guidelines on how to derive reference values (CLSI EP 28-A3c), and report biological variation data (Aarsand et al., Clin Chem 64:3, 501-514, 2018)
- Who are potential partners we could link up with, i.e. existing organizations working towards harmonization and standardization such as IFCC, EFLM, AACB, CDC, MSACL etc., and importantly the potential end-users in testing (Laboratory Medicine, Mayo clinic, ARUP, LabCorp etc.), perhaps commercial entities providing solutions i.e. manufacturer of kits, calibrators and reference materials.
- Vehicles for communication and continuous input: carousel of international research events/conferences that will be used to follow up on outcomes of short workshops such as this one.

Day 1

09:30	*10:00*	*Coffee: Get to know each other*
10:00	11:00	Introduction of status quo and workshop aims - List the current status of plasma lipidomics and identify potentially suitable methods - Reach consensus regarding workflows suitable for harmonized multicentre plasma lipidomics
11:00	12:00	Overview of necessity of reference values - Perspective from Laboratory Medicine (Michael Vogeser) - Discussion: Value of establishing RV to the lipidomics community
12:00	*13:00*	*Lunch (on site)*
13:00	14:30	**Aim 1 – Candidate Lipids** - Identify lipids of potential clinical interest (i.e. Fatty acids, Ceramides, Sterols, TG, LPC, etc) - Decide on a priority list of plasma lipids for which reference values should be developed
14:30	16:00	**Aim 1** (continued) **– Technical details of potential workflows** - Harmonized method across sites (SOPs of "common" methods) vs. lab-specific protocols - Commutable Reference materials (John Bowden) - Internal standards (Paul Baker)
16:00	*16:30*	*Break and Review of Notes and preparation for VIDEO meetings via web-links*
16:30	18:30	VIDEO web-links - Inputs from off-site participants on day 1 workshop proceedings
19:00		*Dinner*

Day 2

09:30	11:00	**Aim 2 – Study populations** - Examples of challenging populations (Andrej Shevchenko) - Priority list of target populations (i.e. pediatric, adult vs geriatric; ethnicities; gender; etc) - Inclusion/exclusions criteria for selection/partitioning of subjects - Identification of potential cohorts
11:00	12:00	**Aim 2** (continued) **- Review of existing guidelines & protocols for estimating RV** - Population sample sizes - Direct sampling vs biobanks
12:00	*13:00*	*Lunch (on site)*
13:00	15:00	**Aim 3 – Roadmap** - Outline potential Work Packages (Lipids/Method/Cohorts) - Discussing potential partners (Clinical, Industry, Metabolomics, Data)
15:00	*15:30*	*Break*
15:30	17:30	VIDEO web-links - Review of Roadmap with off-site participants - Formation of Working Groups for individual Work Packages - Channels for follow-up discussions and decisions: upcoming "Carousel" of meetings, ad-hoc events