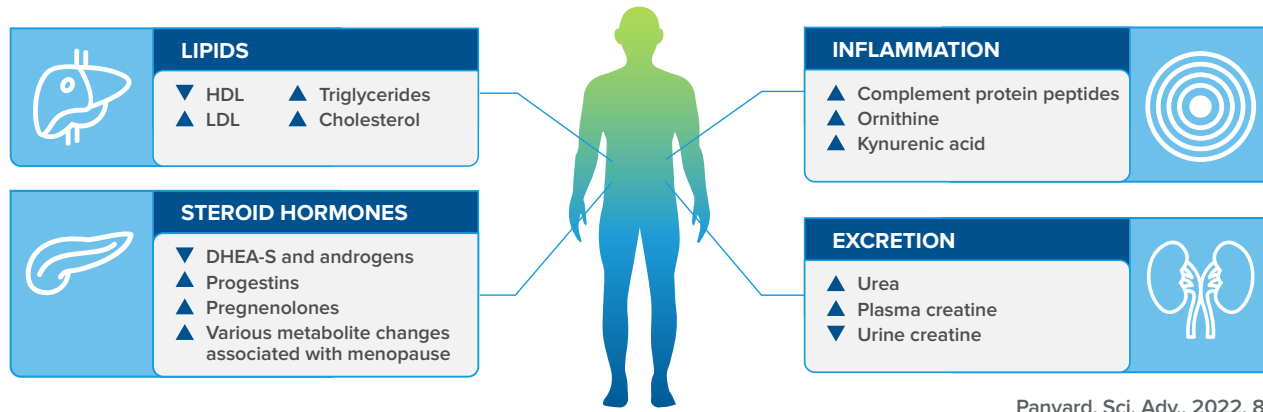




WHITE PAPER

Metabolomics of Aging in Animal Models

The Study of Aging Using Metabolomics in Animal Models



There is a focus in current research on aging through the use of metabolomics and, as would be expected, a great deal of study has examined aging in animal models. One primary driver is simply to understand the underlying mechanisms of aging. By studying the changes in metabolites that occur with aging in animal models, researchers can gain a better understanding of the metabolic pathways and molecular mechanisms that drive age-related declines in health. Metabolomics creates the opportunity to identify potential therapeutic targets for intervention that could help slow or reverse age-related disease.

There is a large focus in aging research on the discovery of biomarkers, which are the specific metabolic signatures that are associated with the aging process. Biomarkers discovered in aging animal models can be used to track changes in health over time and monitor the effectiveness of potential interventions. Thus metabolomics can be used to study the effects of interventions, such as diet, exercise, or pharmacological treatments, on aging in animal models, with the overall goal being that metabolomics data can help to develop more effective interventions to slow or reverse age-related declines in health.

Overall, studying aging in animal models using metabolomics can provide important insights into the underlying mechanisms of aging and the metabolic pathways that are affected by aging, as well as helping to identify potential therapeutic targets and biomarkers of aging.

In order to understand the use of “animal models” for aging research, it helps to understand exactly what is being examined. Various types of biological samples can be collected for metabolomics analysis.

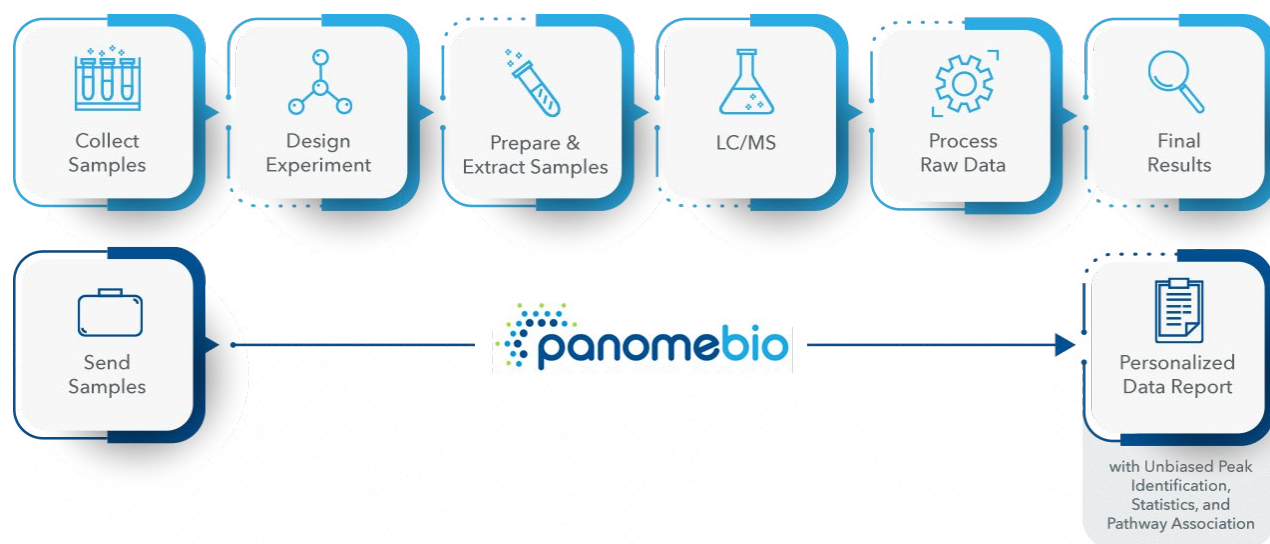
- **Blood is a commonly used sample for metabolomics studies, as it contains a large number of different metabolites that can provide information about the health of an organism.**
- **Blood samples can be easily collected from most animal models, serum or plasma easily isolated, and can be readily used to study changes in metabolites associated with aging.**
- **Urine is another common sample used for metabolomics studies, as it contains a wide range of metabolic waste products that can provide important information about the metabolic state of an organism.**
- **Tissue samples, such as liver, brain, or muscle, are also often used to study the effects of aging in specific tissues and to identify metabolites that are specifically associated with aging in these tissues.**
- **CSF can be collected from the spinal cord and is often used to study aging in the brain and to identify potential biomarkers of age-related neurological diseases.**
- **Saliva is a non-invasive sample that can be easily collected and is increasingly being used for metabolomics studies, including studies of aging.**

In general, the choice of sample will depend on the research question being studied and the type of information that is desired. For example, if the goal is to study changes in metabolites associated with aging in the entire organism, a blood sample might be the most appropriate choice. However, if the goal is to study changes in metabolites in a specific tissue, a tissue sample would be more appropriate.

The importance of animal models in metabolomics-based aging research, and specifically the choice of the right animal model, can be seen in a recent publication by Patrick Pann and colleagues (Pann et al., *Mouse Age Matters: How Age Affects the Murine Plasma Metabolome*, *Metabolites*, 2020) where metabolic differences were identified in the plasma of mice not only when examining age, but also when taking strain into account. Four different strains were examined, including B6J (the most widely utilized inbred mouse strain for all of research), B6NTac (the preferred strain of the Knockout Mouse Project and International Mouse Phenotyping Consortium), 129S1 (the most commonly used transgenic strain) and the C3Fe (the most broadly utilized strain for immunological research). Age-related changes within a strain of mice were noted for every strain and included metabolites such as phosphatidylcholines, methionine, acylcarnitine and hexoses. Perhaps more surprising was the ability for the researchers to identify distinct and unique metabolomic signatures for aging within each strain of mouse. The authors note that “PCA revealed distinct clusters for each mouse strain, indicating the existence of specific metabolite profiles” as early as six weeks of age and thus conclude that caution is advised when comparing metabolomics results of genetically similar substrains.

The outcome of metabolomics research is dependent on the proper collection of samples, strict adherence to experimental procedures, accurate data gathering, preparation and validation, data analysis and integration with other data sets, and the proper identification of relevant metabolites. Metabolomics research creates a significant amount of data, similar to other ‘omics techniques, making it a resource-intensive exercise to extract relevant information. Analyzing and integrating data remains a challenging aspect of uncovering the connections between biological elements and understanding the intricate metabolic processes associated with aging. But while the challenge is significant, the opportunity is enormous to discover aging biomarkers, create aging pharmaceutical interventions, and impact the overall understanding of the aging process through use of metabolomics in animal model systems.

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