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Metabolomics studies to reflect changes in phenotype during stem cell differentiation

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Stem cells respond to a wide variety of physical and chemical cues in their microenvironment. These cues are known to be able to instigate differentiation of stem cells, subsequently developing into specialized cells (bone, fat, muscle and cartilage). *In vivo*, chemical and physical cues in the microenvironment act in cohort with one another to bring about differentiation. While this process is not perfectly understood to be able to replicate *in vitro*, we are able to understand how each cue in their own right is able to influence lineage specification of stem cells on differentiation. During the differentiation process, the metabolic activity of stem cells changes from relative quiescence to high bioactivity. This produces an array of divergent cell behavior that ultimately result in the formation of bone or adipose cell for example. By using a metabolomics-based approach, we are able to study the phenotype of stem cells as they differentiate and form their resultant cell type. Particularly, it offers a way of monitoring innate cell behavior without chemical bias, as is required in some cell culture systems. This has allowed discovery of naturally occurring bioactive metabolites that are central in differentiation as well as being able to distinguish between sub-phenotypes of a singular tissue type. To this end, the information acquired from these divergent metabolomes play an important role in how the subsequent generation of biomaterials are designed, improved and developed for tissue engineering applications.

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