\subsection{Aims}

OPTION A:

In the context of technological advances in the epigenetic, transcriptomic and proteomic fields, a comprehensive multi-omic study in PsA samples to investigate discrete cell populations in circulation and at the site of inflammation has not yet been conducted. This chapter aims to perform a pilot/proof of concept multi-omics study integrating epigenetics, gene expression and single cell transcriptomics and proteomic data from SF and PB in PsA samples in order to deepen in the understanding of cell and tissue specific differences contributing to PsA pathophysiology and chronic inflammation and to further inform PsA GWAS association studies.

The specific aims for this chapter are:

\begin{enumerate}

\item [To characterise and identify differences in the chromatin accessibility landscape between SF and PB in CD14$^+$ monocytes, mCD4$^+$, mCD8$^+$ and NK cells isolated from PsA patients.]

\item [To characterise differences in the transcriptomic profiles between SF and PB for relevant immune genes in CD14$^+$ monocytes, mCD4$^+$ and mCD8$^+$ from the same PsA patients.]

\item[To integrate chromatin accessibility and genes expression profiles from SF and PB in those PsA samples.]

\item[To further explore transcriptional differences at the single-cell level in cell types of interest and perform a basic integration with mass cytometry data.]

\item[To conduct fine-mapping for a number of PsA GWAS loci using genotype data and integration with tissue-specific PsA chromatin accessibility maps and publicly available epigenetic and functional data to further narrow down the putative causal SNPs driving such associations.]

\end{enumerate}

OPTION B:

In the context of technological advances in the epigenetic, transcriptomic and proteomic fields, a comprehensive multi-omic study in PsA samples to investigate discrete cell populations in circulation and at the site of inflammation has not yet been conducted. This pilot study aims to develop a framework for the integration of a mutli-omic dataset in PsA blood and synovial immune cells. Specifically, using the chromatin accessibility landscape and the transcriptomic profile in a number of immune relevant genes in four cell populations isolated from SF and PB to improve the understanding of cell and tissue-specific differences and the relationship between chromatin accessibility and gene expression in PsA. Moreover, single-cell transcriptomic and mass cytometry will attempt to identify common and tissue-associated cell subsets contributing to pathophysiological relevant pathways in PsA and chronic inflammation. Lastly, fine-mapping of PsA GWAS loci and integration with chromatin accessibility maps of relevant immune cells from PsA samples will be performed to further narrow down the putative causal variants driving such associations.

The specific aims for this chapter are:

\begin{enumerate}

\item [To characterise and identify differences in the chromatin accessibility landscape between SF and PB in CD14$^+$ monocytes, mCD4$^+$, mCD8$^+$ and NK cells isolated from PsA patients.]

\item [To characterise differences in the transcriptomic profiles between SF and PB for relevant immune genes in CD14$^+$ monocytes, mCD4$^+$ and mCD8$^+$ from the same PsA patients.]

\item[To integrate chromatin accessibility and genes expression profiles from SF and PB in those PsA samples.]

\item[To further explore transcriptional differences at the single-cell level in cell types of interest and perform a basic integration with mass cytometry data.]

\item[To conduct fine-mapping for a number of PsA GWAS loci using genotype data and integrate with cell and tissue-specific PsA chromatin accessibility maps and publicly available epigenetic and functional data to further narrow down the putative causal SNPs driving such associations.]

\end{enumerate}