

D Improving Soluble Signal Phrasing



please, I need help with improving phrasing:

`\item\textbf{Soluble signals:}` The role of cytokines and chemokines `\dashed{such as MIP-1 α , MCP-1, IL-8, and CXCL12/SDF-1}` in influencing MM adhesion within the BM is well established `\cite{aggarwalChemokinesMultipleMyeloma2006, alsayedMechanismsRegulationCXCR42007}`. For instance, myeloma cells overexpress MIP-1 α constitutively, reducing adhesion and triggering migration in an autocrine fashion `\cite{lentschMacrophageInflammatoryProtein2003, abeRoleMacrophageInflammatory2002}`. When expressed constitutively, these signals could prime MM for detachment. Also, if such signals accumulate and pass a certain threshold, one could assume that they cause detachment as a timely isolated trigger.



Here is an improved version of the phrasing:

`\item\textbf{Soluble signals:}` Cytokines and chemokines, such as MIP-1 α , MCP-1, IL-8, and CXCL12/SDF-1, play a well-established role in influencing MM adhesion within the bone marrow (BM) `\cite{aggarwalChemokinesMultipleMyeloma2006, alsayedMechanismsRegulationCXCR42007}`. For instance, myeloma cells constitutively overexpress MIP-1 α , which reduces adhesion and triggers migration in an autocrine manner `\cite{lentschMacrophageInflammatoryProtein2003, abeRoleMacrophageInflammatory2002}`. Constitutive expression of these signals may prime MM cells for detachment. Additionally, if the accumulation of these signals surpasses a certain threshold, it is reasonable to assume they could act as an isolated trigger for detachment.



ok, can you now help me improve phrasing for this paragraph?

`\textbf{Introducing Adhesion Dramatypes:}`
`\acf{CAD}\footref{foot:cad}` characterizes the time-dependent changes in cell adhesion and detachment, associating these phases with molecular signatures like `\ac{CAM}` expression or cell signaling mediated by the microenvironment. Focusing on a time component is especially useful for predicting the behavior of suspension cells with intricate attachment and detachment behaviors like `\INA`. In that sense, `\MAina` and `\nMAina` are two distinct `\textit{in vitro}` adhesion dramatypes. The adhesion dramatype of `\MAina` cells is characterized by adhesion

factor expression and stable heterotypic adhesion to \acp{hMSC}. This addresses the retention and colonization steps during the multistep-model of dissemination. \MAina cells then transition into another adhesion dramatype \nMAina through cell division and loss of MSC adhesion, and is characterized by unstable homotypic aggregation from which single cells detach. This could represent the release step of dissemination.



Here is the improved version of the paragraph:

Introducing Adhesion Dramatypes: The concept of \ac{CAD}\footref{foot} describes the time-dependent changes in cell adhesion and detachment, linking these phases to molecular signatures such as \ac{CAM} expression or microenvironment-mediated cell signaling. Emphasizing the time component is particularly useful for predicting the behavior of suspension cells with complex attachment and detachment dynamics, such as \INA. In this context, \MAina and \nMAina represent two distinct \textit{in vitro} adhesion dramatypes. The \MAina dramatype is characterized by the expression of adhesion factors and stable heterotypic adhesion to \acp{hMSC}, addressing the retention and colonization steps in the multistep model of dissemination. \MAina cells then transition to the \nMAina dramatype through cell division and the loss of MSC adhesion, characterized by unstable homotypic aggregation from which single cells detach. This may represent the release step in the dissemination process.



Ok, now please improve phrasing for this paragraph:

Distinguishing Phenotype and Dramatype: \INA cells exhibited great reactivity to \acp{hMSC}. Describing this new state as a \emph{phenotype} would correctly imply the influence of both genetic and environmental factors. However, this overloads the term \emph{environmental factors}, as it includes the history of the donor, \textit{in vitro} culturing conditions, the experimental model simulating the \ac{BMME}, and experimental conditions such as the ratio of \acp{MSC} to \INA cells. Animal studies faced a similar issue and hence coined the term \emph{dramatype} % \footquote{\footdramatype}{zutphenPrinciplesLaboratoryAnimal2001} \cite{zutphenPrinciplesLaboratoryAnimal2001}: The dramatype describes the state that is due to proximate environmental factors, whereas the phenotype summarizes the overall environmental background prior to entering that proximate environment. Cancer research uses the term dramatype rarely \cite{hinoStudiesFamilialTumors2004}, or use combinations like \emph{phenotype switching} \cite{woutersRobustGeneExpression2020}. However, such use of terminology blurs the distinction between clonal heterogeneity and transient cell signaling. The author proposes \emph{dramatypes} as a term used in cell biology to focus on transient states available within the bounds of transcriptional plasticity, while \emph{phenotypes} describe relatively persistent genetic and epigenetic backgrounds. These \emph{dramatypes} could

then define distinct adhesive behaviors of myeloma cells observed for each step of dissemination, given the microenvironmental and adhesional changes faced.



Here is the improved version of the paragraph:

Distinguishing Phenotype and Dramatype: INA cells exhibited significant reactivity to hMSC . Describing this new state as a *phenotype* would correctly imply the influence of both genetic and environmental factors. However, this usage overloads the term *environmental factors*, encompassing the donor's history, *in vitro* culturing conditions, the experimental model simulating the BMME , and experimental conditions such as the ratio of MSC to INA cells. Animal studies faced a similar issue and thus introduced the term *dramatype* [\(Zutphen Principles Laboratory Animal 2001\)](#). A dramatype describes the state resulting from immediate environmental factors, while a phenotype summarizes the overall environmental background prior to encountering that environment. In cancer research, the term dramatype is rarely used [\(Hino Studies Familial Tumors 2004\)](#), with some researchers preferring terms like *phenotype switching* [\(Wouters Robust Gene Expression 2020\)](#). This blurs the distinction between clonal heterogeneity and transient cell signaling. The author proposes using *dramatypes* in cell biology to focus on transient states within the bounds of transcriptional plasticity, while *phenotypes* describe relatively persistent genetic and epigenetic backgrounds. These *dramatypes* could then define distinct adhesive behaviors of myeloma cells observed at each step of dissemination, considering the microenvironmental and adhesional changes encountered.



ok, can you now improve this paragraph?

```
\newcommand{\cadddiversity}{%
  \textbf{\ac{CAD} is highly diverse between myeloma patients.} While
  transcriptional plasticity and clonal heterogeneity introduce variance
  into myeloma cell populations, these ?? are influenced by patient-specific
  factors such as disease stage and genomic background. At this point, one
  can assume somewhat unlimited combinations of such factors , leading to
  very different manifestations of \ac{CAD} and dissemination mechanisms
  between patients.}
```



Here is the improved version of the paragraph:

```
\newcommand{\cadddiversity}{%
  \textbf{\ac{CAD} is highly diverse among myeloma patients.} Transcriptional plasticity and clonal
  heterogeneity introduce significant variability into myeloma cell populations. These variations are
```

further influenced by patient-specific factors such as disease stage and genomic background. Consequently, the combinations of these factors can lead to a wide range of manifestations of \ac{CAD} and differing dissemination mechanisms among patients.

}

ChatGPT kann Fehler machen. Überprüfe wichtige Informationen.