Contents

Abbreviations

Introduction

Multiple Myeloma and Other Monoclonal Gammopathies

Multiple Myeloma (MM) is a hematological malignancy characterized by the clonal expansion of malignant plasma cells primarily within multiple sites of the Bone Marrow (BM). This cancer arises from plasma cells, the antibody-producing cells of the immune system, which undergo malignant transformation resulting in uncontrolled growth and disruption of normal bone marrow function (P. Yang et al., 2022). The prevalence of multiple myeloma has tripled across both europe and USA from 1980 to 2014 due to an ageing population (Ocias et al., 2016; Turesson et al., 2018). For 2024, 35780 new MM cases and 12540 deaths are estimated for the USA alone (Siegel et al., 2024).

To understand the progression of a healthy plasma cell to MM, one can review other *monoclonal gammopathies*. These are defined by the presence of monoclonal immunoglobulin in the blood serum which is indicative of abnormal plasma cell clones overexpressing the same type of dysfunctional antibody. (Kyle, 1997; Fermand et al., 2018). When no further disease manifestations are present, the condition is termed *Monoclonal Gammopathy of Undetermined Significance* (MGUS), which is the most commonly diagnosed monoclonal gammopathy (Kyle, 1997). MGUS has a 1-5 % annual risk of progression to MM (Rajkumar et al., 2014).

To distinguish MM from other monoclonal gammopathies, diagnosis of MM requires not only identification of a minimum of clonal plasma cells, but also a *myeloma defining event* which is evidence of malignancy or end-organ damage, such as hypercalcemia, renal insufficiency, anemia, or bone lesions (Rajkumar et al., 2014). A localized smaller[1] mass of clonal plasma cells together with a singular primary bone lesion is diagnosed as Solitary Plasmacytoma (SP). SP can progress to MM in 32 % of cases with a median follow-up of 9.7 years (Thumallapally et al., 2017; S. Gao et al., 2024). Studies from Kyle (1997) show that SP cases are rare, constituting only 2.5 % of monoclonal gammopathy diagnoses, whereas MM represent 18 %. Another rare precursor of MM is *smouldering* or *asymptomatic Multiple Myeloma* (aMM), representing 3 % of monoclonal gammopathies (Kyle, 1997). aMM is diagnosed when no myeloma defining event is detected, although the quantities of clonal plasma cells or monoclonal protein align with respective criteria for MM diagnosis. (Rajkumar et al., 2014). Recent reports show that if left untreated, 72 % of aMM patients progress to MM, whereas early treatment can lower the progression rate to 11 % within up to 7.6 years until last follow-up[2] (Abdallah et al., 2024; Mateos María-Victoria et al., 2013). MM itself can progress to advanced stages, such as *extramedullary involvement/disease* which describes colonization of soft tissues outside the bone marrow (Bladé et al., 2022), but also Plasma Cell Leukemia (PCL) which is characterized by high

[1] Rajkumar et al. (2014): *"Solitary plasmacytoma with 10 % or more clonal plasma cells is regarded as multiple myeloma. [...] If bone marrow has less than 10 % clonal plasma cells, more than one bone lesion is required to distinguish [MM] from solitary plasmacytoma with minimal marrow involvement."*

[2] For non-high risk aMM patients, treatment lowered MM progression rate to 9 %, compared to 31 % for untreated patients (within up to 6.7 and 7.6 years of follow-up, respectively). For high-risk aMM patiens, treatment lowered aMM progression rate to 11 %, compared to 72 % for untreated patients (within up to 5.2 years of follow-up and median time to progression of 2.2 years, respectively) (Abdallah et al., 2024).

levels of circulating plasma cells (Jung & Lee, 2022). However, the most common cause of death is renal failure during the MM stage, caused by excess immunoglobulins or hypercalcemia due to bone degradation (Kundu et al., 2022).

With a 5-year surival rate of 50 % (Turesson et al., 2018), MM can be considered incurable and deadly. MM relapses within the first year in 16 % of patients [Multiple Myeloma Relapse (MMR)], others face relapse at a later time or only continued response to treatment (Majithia et al., 2016). Although treatments have improved, the age-adjusted mortality rate of MM has decreased from 1999 to 2020 by only −1.6 % (Doddi & Rashid, 2024). Engelhardt et al. (2024) describes the current standard care for transplant-eligible newly diagnosed MM patients as follows: Induction with a CD38 antibody, proteasome inhibitor, immunomodulatory drug, and dexamethasone, potentially followed by bone marrow transplantation and lenalidomide maintenance (Rajkumar & Kumar, 2020). A major challenge to these treatments is the continued cycle of remission and relapse, with each relapse generally being harder to treat (Podar & Leleu, 2021). Development of such resistance is well described in the literature, often arising from the intraclonal genetic heterogeneity within the myeloma cell population and the protective niche provided by the Bone Marrow Microenvironment (BMME) (Solimando et al., 2022).

Dissemination of Myeloma Cells

As the name suggests, *multiple* myeloma involves spreading of clonal plasma cells in multiple sites within the body, a process that's described with the term *dissemination*. Although a single large plasmacytoma is still classified as MM (Rajkumar et al., 2014), the presence of multiple tumor lesions within the BM is very common. More than one or 25 such lesions predict poor prognosis for asymptomatic and symptomatic MM patients, respectively (Kastritis et al., 2014; Mai et al., 2015). Additionally, MM cells can disseminate to extramedullary sites of virtually any tissue, highlighting MM as a systemic disease with potential multi-organ impact (Rajkumar & Kumar, 2020; Bladé et al., 2022). Hence, dissemination is a major contributor to MM progression and poor prognosis, enabling MM cells to colonize new niches that favor survival, quiescent states or are less accessible for therapy, especially with high subclonal heterogeneity (Forster & Radpour, 2022; Keats et al., 2012).

Dissemination of MM is reminiscent of *metastasis*, a term typically associated with solid tumors describing the spread of cancer cells to distant sites. However, it substantially differs from metastasis due to the hematological or "liquid" nature of MM. Long-lived plasma cells originate from migratory B-cells, negating the need for extensive transformative processes such as Epithelial-Mesenchymal Transition (EMT), which is required for escaping tightly connected solid tissues to enter the bloodstream (Ribatti et al., 2020). Although referred to as "liquid tumor", MM cells still accumulate as distinct foci within the bone marrow, somewhat mirroring the localized growth of solid tumors. This characteristic has led to MM being proposed as a model for studying solid "micrometastases" (Ghobrial, 2012), highlighting its unique blend of liquid and solid tumor properties and providing insights

into the mechanisms of cancer dissemination and colonization of new niches.

The exact mechanism of MM dissemination is not entirely understood. Nevertheless, attempts to structure this process have been made by Zeissig et al. (2020), describing MM dissemination in five steps:

1. Retention in the BM
2. Release from the BM
3. Intravasation
4. Extravasation
5. Colonization.

According to Zeissig et al. (2020), MM dissemination begins with MM cells overcoming retention and adhesion within the BMME. Following release, MM cells undergo *intravasation* into the bloodstream, where they can circulate before extravasating into new BM sites. This migration is directed by chemokines and growth factors produced by BM cells. For instance, CXCL12 and IGF-1 are critical in guiding MM cells back to the BM, a process called *homing* (Vande Broek et al., 2008). In the BM they can *colonize* and form new tumor foci.

The review by Zeissig et al. (2020) implies a sequential order of such steps, yet direct proof of this is lacking. Still, the review provides a framework that integrates multiple complex research topics into one coherent context. For instance, Zeissig et al. (2020) states that two adhesive processes are critical for succesful dissemination: Lowered adhesion to the BM, but increased adhesion to the endothelium to initiate extravasation (Asosingh et al., 2001; Mrozik et al., 2015). This alone implies stringent separation of different adhesive processes during the dissemination process. Given that Cell Adhesion Molecules (CAMs) have become attractive targets for treating MM (Bou Zerdan et al., 2022; Katz, 2010), such detailed understanding of cell adhesion is crucial for developing successful therapies.

Retention of Myeloma Cells in the Bone Marrow

According to Zeissig et al. (2020), overcoming retention and adhesion to the BME is critical to MM dissemination. Retention of plasma cells to the BME is mediated by multiple mechanisms, which are categorized here into *direct adhesion*, *soluble survival factors* and *chemotaxis*. A fourth notable mechanism is the physical boundary that is bone tissue and Extracellular Matrix (ECM), which could become important for MM dissemination once degradation of bone tissue has progressed.

Direct adhesion of MM cells to the BM is mediated through ECM components and cell adhesion to other BM resident cells like osteoblasts, osteoclasts and Bone Marrow Stromal Cells (BMSCs) (Teoh & Anderson, 1997; Bou Zerdan et al., 2022). ECM components include fibronectin, collagens, and proteoglycans such as decorin (Hu et al., 2021; Huang et al., 2015; Katz, 2010; Kibler et al., 1998). BMSCs are vital in this niche, supporting cell adhesion through CAMs but also by secretion of (ECM)

components (Katz, 2010). Such adhesion acts both as physical anchorage but also provides signaling cues for growth, survival, and drug resistance (Chauhan et al., 1996). A classic example is the binding of MM cell integrins to VCAM-1 on BMSCs, such as 4 1 (VLA-4) (Bou Zerdan et al., 2022). Since direct adhesion promotes both retention and tumour growth, it could play an ambiguous role during MM dissemination.

Soluble survival factors contribute to BM retention, since plasma cells can not survive outside the bone marrow without them. For example, deleting BCMA — a receptor for survival factors — leads to loss of Bone Marrow Plasma Cells (BMPCs) due to unsustained maintenance of cell survival (O'Connor et al., 2004). Soluble survival factors include IL-6, IGF-1, BAFF, APRIL, and VEGF, although IGF-1 has proven to be the primary survival factor (Sprynski et al., 2009). These signals are secreted by BMSCs and adipocytes (Kibler et al., 1998; García-Ortiz et al., 2021). *Chemotaxis* is also crucial for BM retention. CXCL12 and CXCL8 are soluble chemotactic signals produced by BMSCs and attract MM cells, but also primes their cytoskeleton and integrins for adhesion (Aggarwal et al., 2006; Alsayed et al., 2007).

Together, BMSCs play a critical role in MM retention, providing direct adhesion, soluble survival factors, and chemotactic signals.

Release of Myeloma Cells from the Bone Marrow

Zeissig et al. (2020) describes the release of myeloma cells from the BMME as all steps required for overcoming bone marrow retention, but also putative triggers leading to migration out of the BME. To the author's knowledge, release of MM cells is the least understood among disseminative processes. Still, in order to gain understanding of how MM dissemination is initiated, one can summarize reports that could be involved.

Studies suggest that CAMs expression indeed plays a role in MM dissemination. For instance, studies demonstrate that circulating MM cells exhibit reduced levels of integrin $\alpha 4\beta 1$, in contrast to those located in the BM (Paiva et al., 2013, 2011). Given that dissemination can be induced in mice by overexpressing the CAM shedding protease heparanase (Y. Yang et al., 2005), it seems reasonable that dynamic loss of adhesive strength is causing release of MM cells from the BM. Another useful comparison is that of CAMs expression at different disease stages, indicative of their role in disease progression, which in turn could serve as a proxy for dissemative potential. For example, Terpos et al. (2016) reported an increase in adhesion molecule expression of ICAM-1 and VCAM-1 in patients with MM compared to those with MGUS and aMM. However, Pérez-Andrés et al. (2005) reported that CD40 is downregulated in PCL patients, hence, different CAMs could serve ambiguous roles in MM progression. Together, the regulation of CAMs can depend on both momentary microenvironmental factors, but also on the stage of the disease, while the specific stimuli regulating their expression

are not fully defined. A study from Akhmetzyanova et al. (2020) presents CD138 (*aka* Syndecan-1) as a potential *switch* between adhesion and release, as mice treated with CD138 blocking antibodies exhibited rapid mobilization of MM cells from the BM to peripheral blood, confirming that alterations in adhesion molecule expression are sufficient to cause MM cell release. Brandl et al. (2022) builds on that finding, showing that JAM-C inversely correlates with CD138 expression while promoting MM progression in a mouse model.

Another often overlooked requirement for MM cell release is the need for independence from essential growth and survival signals provided by BMSC. Autocrine signaling has been proposed as a key mechanism through which myeloma cells gain independence from essential survival factors such as IL-6 (Frassanito et al., 2001; Urashima et al., 1995). Autocrine signaling could also disrupt responsiveness to Mesenchymal Stromal Cell (MSC)-derived chemotactic signals, since MM cells from BM biopsies were shown to express CXCL12 under hypoxic conditions induced by HIF-2α (Martin et al., 2010). Since MM niches turn increasingly hypoxic and circulating myeloma cells upregulate hypoxia associated genes, hypoxia is a promising factor for understanding the release of MM (Garcés et al., 2020).

The degradation of bone tissue could also play a critical role in myeloma cell release by eliminating adhesive anchorage within the ECM, considering that ECM is remodeled even at the MGUS stage Glavey et al. (2017). This degradation is part of a 'vicious cycle' that is well described in osteotropic cancer types and is the key pathway of bone destruction, dissolving bone-resident growth factors like TGF-β that further drive tumor growth (Harada et al., 2021; Siclari et al., 2007; Wang et al., 2019). Notably, it is reasonable to assume that bone destruction drives dissemination by removing physical barriers, yet such concept was not proven yet.

In summary, the release of MM cells from the BM is a complex process that involves dynamic regulation of CAMs, autocrine signaling, and hypoxia, but also the degradation of bone tissue. These processes are not fully understood and require further investigation to formulate strategies that prevent uncontrolled spread of MM cells and support modern therapies.

MSCs: Mesenchymal Stromal (Stem) Cells

The previous sections mentioned MSCs several times as BMSCs, being a crucial component of the BMME in the context of multiple myeloma (Mangolini & Ringshausen, 2020). Before discussing their role in MM specifically, it is important to understand what an MSC is and what impact this cell type has on biomedical research.

Explaining what an MSC is, can be challenging. MSCs are derived from multiple different sources, serve a wide array of functions and are always isolated as a heterogenous group of cells. This makes it particularly challenging to find a consensus on their exact definition, nomenclature, exact function

and *in vivo* differentiation potential. Therefore, the following paragraphs provide a brief overview of the biology of MSCs set within a historical context.

MSCs first gained popularity as a stem cell. Stem cells lay the foundation of multicellular organisms. Embryonic stem cells orchestrate the growth and patterning during embryonic development, while adult stem cells are responsible for regeneration during adulthood. The classical definition of a stem cell is that of a relatively undifferentiated cell that divides asymmetrically, generating one daughter cell with maintained stemness, and one differentiated daughter cell (Cooper, 2000; Shenghui et al., 2009). Because of their significance in biology and regenerative medicine, stem cells have become a prominent subject in modern research. human Mesenchymal Stromal Cells (hMSCs) have been presented as promising candidate in the context of regeneration, given that they feature also intriguing immunomodulatory capabilities, easy isolation and *in vitro* expansion, and safety for both autologous and allogeneic transplantation (Ullah et al., 2015).

Mesenchyme first appears in embryonic development during gastrulation. There, cells that are committed to a mesodermal fate, lose their cell junctions and exit the epithelial layer in order to migrate freely. This process is called epithelial-mesenchymal transition (Tam & Beddington, 1987; Nowotschin & Hadjantonakis, 2010). Hence, the term mesenchyme describes non-epithelial embryonic tissue differentiating into mesodermal lineages such as bone, muscles and blood. Interestingly, it was shown nearly twenty years earlier that cells within adult bone marrow seemed to have mesenchymal properties as they were able to differentiate into bone tissue (A. J. Friedenstein et al., 1966; A. Friedenstein & Kuralesova, 1971; Bianco, 2014). This was the origin of the *"mesengenic process"*-hypothesis: This concept states that mesenchymal stem cells serve as progenitors for multiple mesodermal tissues (bone, cartilage, muscle, marrow stroma, tendon, fat, dermis and connective tissue) during both adulthood and embryonic development (A. Caplan, 1991; A. I. Caplan, 1994). The mesenchymal nature of these cells (termed bone marrow stromal cells: BMSCs) was confirmed later when they were shown to differentiate into adipocytic (fat) and chondrocytic (cartilage) lineages (Pittenger et al., 1999). Since then, the term *"mesenchymal stem cell"* (MSC) has grown popular as an adult multipotent precursor to a couple of mesodermal tissues. MSCs derived from bone marrow (BMSCs) were shown to differentiate into osteocytes, chondrocytes, adipocytes and cardiomyocytes (Gronthos et al., 1994; Muruganandan et al., 2009; Xu et al., 2004). Most impressively, these cells also exhibited ectodermal and endodermal differentiation potential, as they produced neuronal cells, pancreatic cells and hepatocytes (Barzilay et al., 2009; Wilkins et al., 2009; Gabr et al., 2013; Stock et al., 2014).

It was later established that cultures with MSC-like properties can be isolated from *'virtually every post-natal organs and tissues'*, and not just bone marrow (da Silva Meirelles et al., 2006). However, depending on which tissue they originated from, MSCs can differ greatly in their transcription profile and *in vivo* differentiation potential (Jansen et al., 2010; Sacchetti et al., 2016).

Since MSCs are a heterogenous group of cells, they were defined by their *in vitro* characteristics. A

minimal set of criteria are the following (Dominici et al., 2006): First, MSCs must be plastic adherent. Second, they must express or lack a set of specific surface antigens (positive for CD73, CD90, CD105; negative for CD45, CD34, CD11b, CD19). Third, MSCs must differentiate to osteoblasts, adipocytes and chondroblasts *in vitro*. Together, MSCs exhibit diverse differentiation potentials and can be isolated from multiple sources of the body.

Today, the potential in MSCs lies not their stemness, but rather in their immunomodulatory capabilities, which could be the reason why conventionally the *'S'* in MSC stands for *Stromal* instead of *Stem*. Althogh, MSCs are not yet established in routine clinical practice —despite thousands of clinical trials covering most of the human body's organs—, they still are among the most studied cell types and are topic of vast research (Abdelrazik, 2023). MSCs are valued for their very high treatment tolerance, but also as an adaptive platform for modifications to improve their therapeutic effects (D'souza et al., 2015). For example, Chen & Zhou (2022) boldly announced the translation of modified MSCs into the clinical practice of treating ischemic strokes, whereas Moñivas Gallego & Zurita Castillo (2024) conclude that *further studies are needed*, a statement that's ubiquitous in publications on MSCs based therapies[3]. Still, many fields of research benefit from this vast general understanding of MSCs biology, including this work and the study of the BMME in the context of cancer pathologies such as MM.

Molecular Interactions between MSCs Myeloma Cells

As mentioned in previous sections, MSCs are key drivers of MM progression through mediating retention and survival of MM cells in the bone marrow through e.g. cell adhesion and chemoattractaction (Zeissig et al., 2020). However, BMSCs play a far more complex role in the overall pathology of MM (Mangolini & Ringshausen, 2020). Since bone tissue represents a sturdy physical barrier that MM cells might have to overcome to disseminate, it is crucial to revisit the impact that myeloma cells leave on the BMME.

In healthy bone tissue, there's an equilibrium between bone formation and degradation to maintain turnover, repair and remodelling. (Väänänen, 1993): Mesenchymal stromal cells (BMSCs) differentiate into bone forming osteoblasts, while bone degrading osteoclasts are derived from hematopoietic stem cells. Myeloma cells shift the equilibrium of bone turnover towards degradation, leading to Multiple Myleoma related Bone Disease (MBD) (Hideshima et al., 2007). MBD is present in 80% of patients at diagnosis and is characterized by osteolytic lesions, osteopenia and pathological fractures (Terpos et al., 2018).

MM cells establish this shift in bone turnover on multiple levels: They directly stimulate osteoclast

[3]Abdelrazik (2023): *"Altogether, the articles published in this Special Issue raise more questions than they answer, given that most of the conclusions carry the statement* ***'further studies are needed'****."*

activity by secreting MIP1α (Oba et al., 2005), but also indirectly through reprogramming BMSCs by having them produce osteoclast stimulating factor RANKL (Tsubaki et al., 2020). This is mediated by NF-κB signaling, a pathway that's crucial for MM pathology which is activated through direct cell-cell contact between myeloma cells and BMSCs via e.g. VCAM1 (Cippitelli et al., 2023; Roy et al., 2018). NF-κB is activated in both myeloma cells and BMSCs, but with different outcomes: In myeloma cells, NF-κB transduces survival signaling (Roy et al., 2017). BMSCs however react with stress-induced senescence and secretion of multiple factors that drive MM pathology, such as RANKL and components of the Senescence-Associated Secretory Phenotype (SASP) (Chauhan et al., 1996; Fairfield et al., 2020).

Another fundamental factor contributing to bone destruction is the suppresion of osteogenic differentiation of BMSCs by myeloma cells: MM cells secrete DKK1, which inhibits Wnt signaling that otherwise induces the key osteogenic transcription factor RUNX2 (Gaur et al., 2005; Qiang et al., 2008; F. Zhou et al., 2013). Instead, BMSCs are driven towards the adipogenic lineage MM by VCAM1 signaling, with MM cells stabilizing the adipogenic transcription factor PPAR-γ (Dotterweich et al., 2016; Liu et al., 2020). Furthermore, MM inhibit osteogenic differentiation of BMSCs on an epigenetic level (Allegra et al., 2022). Key mediator GFI1, a zinc finger protein activated by TNF-α which recruits the chromatin modifier HDAC1 to the promoter of RUNX2 (D'Souza et al., 2011; Adamik et al., 2017). Intriguingly, the same group was able to prevent activation of GFI1 and rescue osteogenic differentiation by inhibition of p62, an adapter protein involved in autophagy that bridges several signaling pathways, including NF-κB (Adamik et al., 2018). Teramachi et al. (2016) previously treated mice with the same inhibitor XRK3F2, which resulted in bone formation restricted to MM containing bones.

Overall, MSCs are pivotal within the BMME, serving both structural and responsive roles in MM. NF-κB signaling, essential in MSC-myeloma interactions, plays a crucial role in myeloma survival and MSC function modification (Cippitelli et al., 2023; Roy et al., 2018). Direct contact is necessary to activate these pathways, exacerbating MM pathology. Targeting NF-κB offers therapeutic potential, aiming to disrupt key interactions and inhibit myeloma progression. Deeper molecular understanding could lead to therapies that effectively target the cancer microenvironment driving MM progression.

References

Abadi, M., Agarwal, A., Barham, P., Brevdo, E., Chen, Z., Citro, C., … Zheng, X. (2016, March). *TensorFlow: Large-Scale Machine Learning on Heterogeneous Distributed Systems* (No. arXiv:1603.04467). arXiv. Retrieved 2024-03-07, from http://arxiv.org/abs/1603.04467 doi: 10.48550/arXiv.1603.04467

Abdallah, N. H., Lakshman, A., Kumar, S. K., Cook, J., Binder, M., Kapoor, P., … Rajkumar, S. V. (2024, January). Mode of progression in smoldering multiple myeloma: A study of 406 patients. *Blood Cancer Journal*, *14*(1), 1–7. Retrieved 2024-05-22, from https://www.nature.com/articles/s41408-024-00980-5 doi: 10.1038/s41408-024-00980-5

Abdelrazik, H. (2023, August). Mesenchymal Stem Cells: A Hope or a Hype? *International Journal of Molecular Sciences*, *24*(17), 13218. Retrieved 2024-06-10, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10487858/ doi: 10.3390/ijms241713218

Adamik, J., Jin, S., Sun, Q., Zhang, P., Weiss, K. R., Anderson, J. L., … Galson, D. L. (2017, April). EZH2 or HDAC1 Inhibition Reverses Multiple Myeloma-Induced Epigenetic Suppression of Osteoblast Differentiation. *Molecular cancer research: MCR*, *15*(4), 405–417. doi: 10.1158/1541-7786.MCR-16-0242-T

Adamik, J., Silbermann, R., Marino, S., Sun, Q., Anderson, J. L., Zhou, D., … Galson, D. L. (2018). XRK3F2 Inhibition of p62-ZZ Domain Signaling Rescues Myeloma-Induced GFI1-Driven Epigenetic Repression of the Runx2 Gene in Pre-osteoblasts to Overcome Differentiation Suppression. *Frontiers in Endocrinology*, *9*, 344. doi: 10.3389/fendo.2018.00344

Aggarwal, R., Ghobrial, I. M., & Roodman, G. D. (2006, October). Chemokines in multiple myeloma. *Experimental hematology*, *34*(10), 1289–1295. Retrieved 2023-04-02, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3134145/ doi: 10.1016/j.exphem.2006.06.017

Akhmetzyanova, I., McCarron, M. J., Parekh, S., Chesi, M., Bergsagel, P. L., & Fooksman, D. R. (2020). Dynamic CD138 surface expression regulates switch between myeloma growth and dissemination. *Leukemia*, *34*(1), 245–256. Retrieved 2023-04-04, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6923614/ doi: 10.1038/s41375-019-0519-4

Allegra, A., Casciaro, M., Barone, P., Musolino, C., & Gangemi, S. (2022, May). Epigenetic Crosstalk between Malignant Plasma Cells and the Tumour Microenvironment in Multiple Myeloma. *Cancers*, *14*(11), 2597. Retrieved 2024-06-10, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9179362/ doi: 10.3390/cancers14112597

Alsayed, Y., Ngo, H., Runnels, J., Leleu, X., Singha, U. K., Pitsillides, C. M., … Ghobrial, I. M. (2007, April). Mechanisms of regulation of CXCR4/SDF-1 (CXCL12)-dependent migration and homing in multiple myeloma. *Blood*, *109*(7), 2708–2717. doi: 10.1182/blood-2006-07-035857

Anders, S., Pyl, P. T., & Huber, W. (2015, January). HTSeq–a Python framework to work with high-throughput sequencing data. *Bioinformatics (Oxford, England)*, *31*(2), 166–169. doi: 10.1093/bioinformatics/btu638

Andrews, S. (2010). *FASTQC. A quality control tool for high throughput sequence data.*

Arefin, S. E., Heya, T. A., Al-Qudah, H., Ineza, Y., & Serwadda, A. (2023, July). *Unmasking the giant: A comprehensive evaluation of ChatGPT's proficiency in coding algorithms and data structures* (No. arXiv:2307.05360). arXiv. Retrieved 2024-05-03, from http://arxiv.org/abs/2307.05360 doi: 10.48550/arXiv.2307.05360

Armstrong, R. A. (2014, September). When to use the Bonferroni correction. *Ophthalmic & Physiological Optics: The Journal of the British College of Ophthalmic Opticians (Optometrists)*, *34*(5), 502–508. doi: 10.1111/opo.12131

Asosingh, K., Günthert, U., De Raeve, H., Van Riet, I., Van Camp, B., & Vanderkerken, K. (2001). A unique pathway in the homing of murine multiple myeloma cells: CD44v10 mediates binding to bone marrow endothelium. *Cancer Research*, *61*(7), 2862–2865.

Baker, M. (2016, May). 1,500 scientists lift the lid on reproducibility. *Nature*, *533*(7604), 452–454. Retrieved 2024-04-22, from https://www.nature.com/articles/533452a doi: 10.1038/533452a

Bao, L., Lai, Y., Liu, Y., Qin, Y., Zhao, X., Lu, X., … Huang, X. (2013, September). CXCR4 is a good survival prognostic indicator in multiple myeloma patients. *Leukemia Research*, *37*(9), 1083–1088. doi: 10.1016/j.leukres.2013.06.002

Barzilay, R., Ben-Zur, T., Bulvik, S., Melamed, E., & Offen, D. (2009, May). Lentiviral delivery of LMX1a enhances dopaminergic phenotype in differentiated human bone marrow mesenchymal stem cells. *Stem cells and development*, *18*(4), 591–601. doi: 10.1089/scd.2008.0138

Begley, C. G., & Ioannidis, J. P. A. (2015, January). Reproducibility in science: Improving the standard for basic and preclinical research. *Circulation Research*, *116*(1), 116–126. doi: 10.1161/CIRCRESAHA.114.303819

Bianco, P. (2014). "Mesenchymal" stem cells. *Annual review of cell and developmental biology*, *30*, 677–704. doi: 10.1146/annurev-cellbio-100913-013132

Bladé, J., Beksac, M., Caers, J., Jurczyszyn, A., von Lilienfeld-Toal, M., Moreau, P., … Richardson, P. (2022, March). Extramedullary disease in multiple myeloma: A systematic literature review. *Blood Cancer Journal*, *12*(3), 1–10. Retrieved 2023-03-24, from https://www.nature.com/articles/s41408-022-00643-3 doi: 10.1038/s41408-022-00643-3

Blonska, M., Zhu, Y., Chuang, H. H., You, M. J., Kunkalla, K., Vega, F., & Lin, X. (2015, February). Jun-regulated genes promote interaction of diffuse large B-cell lymphoma with the microenvironment. *Blood*, *125*(6), 981–991. Retrieved 2023-03-01, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4319238/ doi: 10.1182/blood-2014-04-568188

Bobin, A., & Leleu, X. (2022, September). Recent advances in the treatment of multiple myeloma: A brief review. *Faculty Reviews*, *11*, 28. Retrieved 2024-03-27, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9523543/ doi: 10.12703/r/11-28

Bolado-Carrancio, A., Rukhlenko, O. S., Nikonova, E., Tsyganov, M. A., Wheeler, A., Garcia-Munoz, A., … Kholodenko, B. N. (2020, July). Periodic propagating waves coordinate RhoGTPase network dynamics at the leading and trailing edges during cell migration. *eLife*, *9*, e58165. Retrieved 2024-04-25, from https://elifesciences.org/articles/58165 doi: 10.7554/eLife.58165

Bondi, A. B. (2000, September). Characteristics of scalability and their impact on performance. In *Proceedings of the 2nd international workshop on Software and performance* (pp. 195–203). New York, NY, USA: Association for Computing Machinery. Retrieved 2024-03-07, from https://dl.acm.org/doi/10.1145/350391.350432 doi: 10.1145/350391.350432

Bosch-Queralt, M., Tiwari, V., Damkou, A., Vaculčiaková, L., Alexopoulos, I., & Simons, M. (2022, March). A fluorescence microscopy-based protocol for volumetric measurement of lysolecithin lesion-associated de- and re-myelination in mouse brain. *STAR protocols*, *3*(1), 101141. doi: 10.1016/j.xpro.2022.101141

Boswell, D., & Foucher, T. (2011). *The Art of Readable Code: Simple and Practical Techniques for Writing Better Code*. "O'Reilly Media, Inc.".

Bou Zerdan, M., Nasr, L., Kassab, J., Saba, L., Ghossein, M., Yaghi, M., … Chaulagain, C. P. (2022). Adhesion molecules in multiple myeloma oncogenesis and targeted therapy. *International Journal of Hematologic Oncology*, *11*(2), IJH39. Retrieved 2023-02-01, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9136637/ doi: 10.2217/ijh-2021-0017

Brandl, A., Solimando, A. G., Mokhtari, Z., Tabares, P., Medler, J., Manz, H., … Beilhack, A. (2022, March). Junctional adhesion molecule C expression specifies a CD138low/neg multiple myeloma cell population in mice and humans. *Blood Advances*, *6*(7), 2195–2206. Retrieved 2023-04-04, from https://doi.org/10.1182/bloodadvances.2021004354 doi: 10.1182/bloodadvances.2021004354

Brankatschk, R., Bodenhausen, N., Zeyer, J., & Bürgmann, H. (2012, June). Simple Absolute Quantification Method

Correcting for Quantitative PCR Efficiency Variations for Microbial Community Samples. *Applied and Environmental Microbiology*, *78*(12), 4481–4489. Retrieved 2023-05-27, from https://journals.asm.org/doi/10.1128/AEM.07878-11 doi: 10.1128/AEM.07878-11

Brooke, J. (1996, January). SUS – a quick and dirty usability scale. In (pp. 189–194).

Bubendorf, L. (2001, August). High-throughput microarray technologies: From genomics to clinics. *European Urology*, *40*(2), 231–238. doi: 10.1159/000049777

Burger, R., Guenther, A., Bakker, F., Schmalzing, M., Bernand, S., Baum, W., … Gramatzki, M. (2001). Gp130 and ras mediated signaling in human plasma cell line INA-6: A cytokine-regulated tumor model for plasmacytoma. *The Hematology Journal: The Official Journal of the European Haematology Association*, *2*(1), 42–53. doi: 10.1038/sj.thj.6200075

Burger, R., Günther, A., Bakker, F., Schmalzing, M., Bernand, S., Baum, W., … Gramatzki, M. (2001, January). Gp130 and ras mediated signaling in human plasma cell line INA6: A cytokine-regulated tumor model for plasmacytoma. *Hematology Journal - HEMATOL J*, *2*, 42–53. doi: 10.1038/sj.thj.6200075

Bustin, S. A. (2014, December). The reproducibility of biomedical research: Sleepers awake! *Biomolecular Detection and Quantification*, *2*, 35–42. Retrieved 2024-03-18, from https://www.sciencedirect.com/science/article/pii/S2214753515000030 doi: 10.1016/j.bdq.2015.01.002

Bustin, S. A., Benes, V., Garson, J., Hellemans, J., Huggett, J., Kubista, M., … Vandesompele, J. (2013, November). The need for transparency and good practices in the qPCR literature. *Nature Methods*, *10*(11), 1063–1067. Retrieved 2024-05-16, from https://www.nature.com/articles/nmeth.2697 doi: 10.1038/nmeth.2697

Caplan, A. (1991). Mesenchymal stem cells. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society*, *9*(5), 641–50. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1870029 doi: 10.1002/jor.1100090504

Caplan, A. I. (1994, July). The mesengenic process. *Clinics in plastic surgery*, *21*(3), 429–435.

Carlson, M. (2016). Org.Hs.eg.db. *Bioconductor*. Retrieved 2023-06-09, from http://bioconductor.org/packages/org.Hs.eg.db/ doi: 10.18129/B9.bioc.org.Hs.eg.db

Chacon, S., & Straub, B. (2024, March). *Git - Book*. Retrieved 2024-03-07, from https://git-scm.com/book/de/v2

Charlier, F., Weber, M., Izak, D., Harkin, E., Magnus, M., Lalli, J., … Repplinger, S. (2022, October). *Trevismd/statannotations: V0.5*. Zenodo. Retrieved 2023-11-16, from https://zenodo.org/record/7213391 doi: 10.5281/ZENODO.7213391

Chatterjee, M., Hönemann, D., Lentzsch, S., Bommert, K., Sers, C., Herrmann, P., … Bargou, R. C. (2002, November). In the presence of bone marrow stromal cells human multiple myeloma cells become independent of the IL-6/gp130/STAT3 pathway. *Blood*, *100*(9), 3311–3318. doi: 10.1182/blood-2002-01-0102

Chauhan, D., Uchiyama, H., Akbarali, Y., Urashima, M., Yamamoto, K., Libermann, T., & Anderson, K. (1996, February). Multiple myeloma cell adhesion-induced interleukin-6 expression in bone marrow stromal cells involves activation of NF-??B. *Blood*, *87*, 1104–12. doi: 10.1182/blood.V87.3.1104.bloodjournal8731104

Chen, H., & Zhou, L. (2022, June). Treatment of ischemic stroke with modified mesenchymal stem cells. *International Journal of Medical Sciences*, *19*(7), 1155–1162. Retrieved 2024-06-10, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9339408/ doi: 10.7150/ijms.74161

Cippitelli, M., Stabile, H., Kosta, A., Petillo, S., Lucantonio, L., Gismondi, A., … Fionda, C. (2023, January). Role of NF-κB Signaling in the Interplay between Multiple Myeloma and Mesenchymal Stromal Cells. *International Journal of Molecular Sciences*, *24*(3), 1823. Retrieved 2024-06-08, from https://www.mdpi.com/1422-0067/24/3/1823 doi: 10.3390/ijms24031823

Codecov. (2024). Retrieved 2024-05-02, from https://github.com/codecov

Committee on Strategies for Responsible Sharing of Clinical Trial Data, Board on Health Sciences Policy, & Institute of Medicine. (2015). *Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk*. Washington (DC): National

Academies Press (US). Retrieved 2024-04-23, from http://www.ncbi.nlm.nih.gov/books/NBK269030/

Cooper, G. M. (2000). The Cell: A Molecular Approach. 2nd Edition. *Sinauer Associates*, Proliferation in Development and Differentiation. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK9906/

da Silva Meirelles, L., Chagastelles, P. C., & Nardi, N. B. (2006, June). Mesenchymal stem cells reside in virtually all post-natal organs and tissues. *Journal of cell science*, *119*(Pt 11), 2204–2213. doi: 10.1242/jcs.02932

Davidson-Pilon, C. (2019, August). Lifelines: Survival analysis in Python. *Journal of Open Source Software*, *4*(40), 1317. Retrieved 2024-05-02, from https://joss.theoj.org/papers/10.21105/joss.01317 doi: 10.21105/joss.01317

Depil, S., Duchateau, P., Grupp, S. A., Mufti, G., & Poirot, L. (2020, March). 'Off-the-shelf' allogeneic CAR T cells: Development and challenges. *Nature Reviews Drug Discovery*, *19*(3), 185–199. Retrieved 2024-03-27, from https://www.nature.com/articles/s41573-019-0051-2 doi: 10.1038/s41573-019-0051-2

Ding, W., Goldberg, D., & Zhou, W. (2023, August). PyComplexHeatmap: A Python package to visualize multimodal genomics data. *iMeta*, *2*(3), e115. doi: 10.1002/imt2.115

Dobin, A., Davis, C. A., Schlesinger, F., Drenkow, J., Zaleski, C., Jha, S., … Gingeras, T. R. (2013, January). STAR: Ultrafast universal RNA-seq aligner. *Bioinformatics*, *29*(1), 15–21. Retrieved 2023-05-27, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530905/ doi: 10.1093/bioinformatics/bts635

Doddi, S., & Rashid, M. H. (2024). Disparities in Multiple Myeloma Mortality Rate Trends by Demographic Status in the USA. *Cancer Diagnosis & Prognosis*, *4*(3), 288–294. doi: 10.21873/cdp.10322

Dominici, M., Le Blanc, K., Mueller, I., Slaper-Cortenbach, I., Marini, F., Krause, D., … Horwitz, E. (2006). Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. *Cytotherapy*, *8*(4), 315–317. doi: 10.1080/14653240600855905

Dotterweich, J., Schlegelmilch, K., Keller, A., Geyer, B., Schneider, D., Zeck, S., … Schütze, N. (2016, December). Contact of myeloma cells induces a characteristic transcriptome signature in skeletal precursor cells -Implications for myeloma bone disease. *Bone*, *93*, 155–166. doi: 10.1016/j.bone.2016.08.006

D'souza, N., Rossignoli, F., Golinelli, G., Grisendi, G., Spano, C., Candini, O., … Dominici, M. (2015, August). Mesenchymal stem/stromal cells as a delivery platform in cell and gene therapies. *BMC medicine*, *13*, 186. doi: 10.1186/s12916-015-0426-0

D'Souza, S., del Prete, D., Jin, S., Sun, Q., Huston, A. J., Kostov, F. E., … Galson, D. L. (2011, December). Gfi1 expressed in bone marrow stromal cells is a novel osteoblast suppressor in patients with multiple myeloma bone disease. *Blood*, *118*(26), 6871–6880. Retrieved 2024-06-08, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3245209/ doi: 10.1182/blood-2011-04-346775

Dunn, W., Burgun, A., Krebs, M.-O., & Rance, B. (2017, November). Exploring and visualizing multidimensional data in translational research platforms. *Briefings in Bioinformatics*, *18*(6), 1044–1056. Retrieved 2024-04-23, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5862238/ doi: 10.1093/bib/bbw080

Duvall, P., Matyas, S., & Glover, A. (2007). *Continuous integration: Improving software quality and reducing risk*. Pearson Education. Retrieved from https://books.google.de/books?id=PV9qfEdv9L0C

Dziadowicz, S. A., Wang, L., Akhter, H., Aesoph, D., Sharma, T., Adjeroh, D. A., … Hu, G. (2022, January). Bone Marrow Stroma-Induced Transcriptome and Regulome Signatures of Multiple Myeloma. *Cancers*, *14*(4), 927. Retrieved 2022-10-25, from https://www.mdpi.com/2072-6694/14/4/927 doi: 10.3390/cancers14040927

Ekmekci, B., McAnany, C. E., & Mura, C. (2016, July). An Introduction to Programming for Bioscientists: A Python-Based Primer. *PLOS Computational Biology*, *12*(6), e1004867. Retrieved 2024-03-10, from https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1004867 doi: 10.1371/journal.pcbi.1004867

Engelhardt, M., Kortüm, K. M., Goldschmidt, H., & Merz, M. (2024, February). Functional cure and long-term survival in multiple myeloma: How to challenge the previously impossible. *Haematologica*. doi: 10.3324/haematol.2023.283058

Evers, M., Schreder, M., Stühmer, T., Jundt, F., Ebert, R., Hartmann, T. N., … Leich, E. (2023, March). Prognostic

value of extracellular matrix gene mutations and expression in multiple myeloma. *Blood Cancer Journal*, *13*(1), 43. doi: 10.1038/s41408-023-00817-7

Ewels, P., Magnusson, M., Lundin, S., & Käller, M. (2016, October). MultiQC: Summarize analysis results for multiple tools and samples in a single report. *Bioinformatics*, *32*(19), 3047–3048. Retrieved 2023-06-09, from https://doi.org/10.1093/bioinformatics/btw354 doi: 10.1093/bioinformatics/btw354

Excel, M. (2023, August). *Announcing Python in Excel: Combining the power of Python and the flexibility of Excel.* Retrieved 2024-03-11, from https://techcommunity.microsoft.com/t5/excel-blog/announcing-python-in-excel-combining-the-power-of-python-and-the/ba-p/3893439

Fairfield, H., Costa, S., Falank, C., Farrell, M., Murphy, C. S., D'Amico, A., … Reagan, M. R. (2020). Multiple Myeloma Cells Alter Adipogenesis, Increase Senescence-Related and Inflammatory Gene Transcript Expression, and Alter Metabolism in Preadipocytes. *Frontiers in Oncology*, *10*, 584683. doi: 10.3389/fonc.2020.584683

Federer, L. M., Lu, Y.-L., & Joubert, D. J. (2016, January). Data literacy training needs of biomedical researchers. *Journal of the Medical Library Association : JMLA*, *104*(1), 52–57. Retrieved 2024-04-24, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4722643/ doi: 10.3163/1536-5050.104.1.008

Fermand, J.-P., Bridoux, F., Dispenzieri, A., Jaccard, A., Kyle, R. A., Leung, N., & Merlini, G. (2018, October). Monoclonal gammopathy of clinical significance: A novel concept with therapeutic implications. *Blood*, *132*(14), 1478–1485. doi: 10.1182/blood-2018-04-839480

Fernandez-Rebollo, E., Mentrup, B., Ebert, R., Franzen, J., Abagnale, G., Sieben, T., … Wagner, W. (2017, July). Human Platelet Lysate versus Fetal Calf Serum: These Supplements Do Not Select for Different Mesenchymal Stromal Cells. *Scientific Reports*, *7*, 5132. Retrieved 2023-05-02, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5506010/ doi: 10.1038/s41598-017-05207-1

Flier, J. S. (2022). The Problem of Irreproducible Bioscience Research. *Perspectives in Biology and Medicine*, *65*(3), 373–395. doi: 10.1353/pbm.2022.0032

Forster, S., & Radpour, R. (2022, July). Molecular Impact of the Tumor Microenvironment on Multiple Myeloma Dissemination and Extramedullary Disease. *Frontiers in Oncology*, *12*. Retrieved 2024-05-23, from https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2022.941437/full doi: 10.3389/fonc.2022.941437

Frassanito, M. A., Cusmai, A., Iodice, G., & Dammacco, F. (2001, January). Autocrine interleukin-6 production and highly malignant multiple myeloma: Relation with resistance to drug-induced apoptosis. *Blood*, *97*(2), 483–489. doi: 10.1182/blood.v97.2.483

Friedenstein, A., & Kuralesova, A. I. (1971, August). Osteogenic precursor cells of bone marrow in radiation chimeras. *Transplantation*, *12*(2), 99–108.

Friedenstein, A. J., Piatetzky-Shapiro, I. I., & Petrakova, K. V. (1966, December). Osteogenesis in transplants of bone marrow cells. *Journal of embryology and experimental morphology*, *16*(3), 381–390.

Gabr, M. M., Zakaria, M. M., Refaie, A. F., Ismail, A. M., Abou-El-Mahasen, M. A., Ashamallah, S. A., … Ghoneim, M. A. (2013). Insulin-producing cells from adult human bone marrow mesenchymal stem cells control streptozotocin-induced diabetes in nude mice. *Cell transplantation*, *22*(1), 133–145. doi: 10.3727/096368912X647162

Gao, D., Ji, L., Bai, Z., Ouyang, M., Li, P., Mao, D., … Shou, M. Z. (2024, January). *ASSISTGUI: Task-Oriented Desktop Graphical User Interface Automation* (No. arXiv:2312.13108). arXiv. Retrieved 2024-05-16, from http://arxiv.org/abs/2312.13108 doi: 10.48550/arXiv.2312.13108

Gao, S., Wang, Y.-T., Ma, G.-Y., Lu, M.-Q., Chu, B., Shi, L., … Bao, L. (2024, April). Solitary bone plasmacytoma: Long-term clinical outcomes in a single center. *Current Problems in Cancer*, *50*, 101095. doi: 10.1016/j.currproblcancer.2024.101095

Garcés, J.-J., Simicek, M., Vicari, M., Brozova, L., Burgos, L., Bezdekova, R., … Paiva, B. (2020, February). Transcriptional profiling of circulating tumor cells in multiple myeloma: A new model to understand disease dissemination.

Leukemia, *34*(2), 589–603. doi: 10.1038/s41375-019-0588-4

García-Ortiz, A., Rodríguez-García, Y., Encinas, J., Maroto-Martín, E., Castellano, E., Teixidó, J., & Martínez-López, J. (2021, January). The Role of Tumor Microenvironment in Multiple Myeloma Development and Progression. *Cancers*, *13*(2). Retrieved 2021-02-02, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7827690/ doi: 10.3390/cancers13020217

Gaur, T., Lengner, C. J., Hovhannisyan, H., Bhat, R. A., Bodine, P. V. N., Komm, B. S., … Lian, J. B. (2005, September). Canonical WNT signaling promotes osteogenesis by directly stimulating Runx2 gene expression. *The Journal of Biological Chemistry*, *280*(39), 33132–33140. doi: 10.1074/jbc.M500608200

Gentleman. (n.d.). *Bioconductor - BiocViews.* Retrieved 2023-06-09, from https://bioconductor.org/packages/3.17/BiocViews.html

Ghobrial, I. M. (2012, July). Myeloma as a model for the process of metastasis: Implications for therapy. *Blood*, *120*(1), 20–30. Retrieved 2022-10-15, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3390959/ doi: 10.1182/blood-2012-01-379024

Giorgi, F. M., Ceraolo, C., & Mercatelli, D. (2022, April). The R Language: An Engine for Bioinformatics and Data Science. *Life*, *12*(5), 648. Retrieved 2024-04-21, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9148156/ doi: 10.3390/life12050648

Glavey, S. V., Naba, A., Manier, S., Clauser, K., Tahri, S., Park, J., … Ghobrial, I. M. (2017, November). Proteomic characterization of human multiple myeloma bone marrow extracellular matrix. *Leukemia*, *31*(11), 2426–2434. Retrieved 2023-09-05, from https://www.nature.com/articles/leu2017102 doi: 10.1038/leu.2017.102

Gomez-Cabrero, D., Abugessaisa, I., Maier, D., Teschendorff, A., Merkenschlager, M., Gisel, A., … Tegnér, J. (2014, March). Data integration in the era of omics: Current and future challenges. *BMC Systems Biology*, *8*(2), I1. Retrieved 2024-03-18, from https://doi.org/10.1186/1752-0509-8-S2-I1 doi: 10.1186/1752-0509-8-S2-I1

Gómez-López, G., Dopazo, J., Cigudosa, J. C., Valencia, A., & Al-Shahrour, F. (2019, May). Precision medicine needs pioneering clinical bioinformaticians. *Briefings in Bioinformatics*, *20*(3), 752–766. doi: 10.1093/bib/bbx144

Goodman, S. N., Fanelli, D., & Ioannidis, J. P. A. (2016, June). What does research reproducibility mean? *Science Translational Medicine*, *8*(341), 341ps12-341ps12. Retrieved 2024-03-18, from https://www.science.org/doi/10.1126/scitranslmed.aaf5027 doi: 10.1126/scitranslmed.aaf5027

Gorelick, M., & Ozsvald, I. (2020). *High Performance Python: Practical Performant Programming for Humans.* "O'Reilly Media, Inc.".

Gosselin, R.-D. (2021, February). Insufficient transparency of statistical reporting in preclinical research: A scoping review. *Scientific Reports*, *11*(1), 3335. Retrieved 2024-03-11, from https://www.nature.com/articles/s41598-021-83006-5 doi: 10.1038/s41598-021-83006-5

Gramatzki, M., Burger, R., Trautman, U., Marschalek, R., Lorenz, H., Hansen-Hagge, T., … Kalden, J. (1994). Two new interleukin-6 dependent plasma cell lines carrying a chromosomal abnormality involving the IL-6 gene locus. , *84 Suppl. 1*, 173a-173a. Retrieved 2023-03-24, from https://www.cellosaurus.org/cellopub/CLPUB00060

GraphPad Prism 10 User Guide. (2024). Retrieved 2024-05-14, from https://www.graphpad.com/guides/prism/latest/user-guide/multiple-variable-tables.htm

Greenstein, S., Krett, N. L., Kurosawa, Y., Ma, C., Chauhan, D., Hideshima, T., … Rosen, S. T. (2003, April). Characterization of the MM.1 human multiple myeloma (MM) cell lines: A model system to elucidate the characteristics, behavior, and signaling of steroid-sensitive and -resistant MM cells. *Experimental Hematology*, *31*(4), 271–282. doi: 10.1016/s0301-472x(03)00023-7

Gronthos, S., Graves, S. E., Ohta, S., & Simmons, P. J. (1994, December). The STRO-1+ fraction of adult human bone marrow contains the osteogenic precursors. *Blood*, *84*(12), 4164–4173.

Hannun, A., Digani, J., Katharopoulos, A., & Collobert, R. (2023). *MLX: Efficient and flexible machine learning on Apple silicon.* Retrieved from https://github.com/ml-explore

Harada, T., Hiasa, M., Teramachi, J., & Abe, M. (2021, September). Myeloma–Bone Interaction: A Vicious Cycle via TAK1–PIM2 Signaling. *Cancers*, *13*(17). Retrieved 2024-06-05, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8431187/ doi: 10.3390/cancers13174441

Harrington, D. P., & Fleming, T. R. (1982). A Class of Rank Test Procedures for Censored Survival Data. *Biometrika*, *69*(3), 553–566. Retrieved 2023-08-07, from https://www.jstor.org/stable/2335991 doi: 10.2307/2335991

Harris, C. R., Millman, K. J., van der Walt, S. J., Gommers, R., Virtanen, P., Cournapeau, D., … Oliphant, T. E. (2020, September). Array programming with NumPy. *Nature*, *585*(7825), 357–362. Retrieved 2023-08-09, from https://www.nature.com/articles/s41586-020-2649-2 doi: 10.1038/s41586-020-2649-2

Hideshima, T., Mitsiades, C., Tonon, G., Richardson, P. G., & Anderson, K. C. (2007, August). Understanding multiple myeloma pathogenesis in the bone marrow to identify new therapeutic targets. *Nature Reviews Cancer*, *7*(8), 585–598. Retrieved 2023-02-07, from https://www.nature.com/articles/nrc2189 doi: 10.1038/nrc2189

Hose, D., Rème, T., Hielscher, T., Moreaux, J., Messner, T., Seckinger, A., … Goldschmidt, H. (2011, January). Proliferation is a central independent prognostic factor and target for personalized and risk-adapted treatment in multiple myeloma. *Haematologica*, *96*(1), 87–95. doi: 10.3324/haematol.2010.030296

Hothorn, T., & Lausen, B. (n.d.). *Maximally Selected Rank Statistics in R.* Retrieved from http://cran.r-project.org/web/packages/maxstat/index.html.

Howe, A., & Chain, P. S. G. (2015). Challenges and opportunities in understanding microbial communities with metagenome assembly (accompanied by IPython Notebook tutorial). *Frontiers in Microbiology*, *6*, 678. doi: 10.3389/fmicb.2015.00678

Hu, X., Villodre, E. S., Larson, R., Rahal, O. M., Wang, X., Gong, Y., … Debeb, B. G. (2021, January). Decorin-mediated suppression of tumorigenesis, invasion, and metastasis in inflammatory breast cancer. *Communications Biology*, *4*(1), 72. doi: 10.1038/s42003-020-01590-0

Huang, S.-Y., Lin, H.-H., Yao, M., Tang, J.-L., Wu, S.-J., Hou, H.-A., … Tien, H.-F. (2015). Higher Decorin Levels in Bone Marrow Plasma Are Associated with Superior Treatment Response to Novel Agent-Based Induction in Patients with Newly Diagnosed Myeloma - A Retrospective Study. *PloS One*, *10*(9), e0137552. doi: 10.1371/journal.pone.0137552

Hunter, J. D. (2007, May). Matplotlib: A 2D Graphics Environment. *Computing in Science & Engineering*, *9*(3), 90–95. Retrieved 2023-11-15, from https://ieeexplore.ieee.org/document/4160265 doi: 10.1109/MCSE.2007.55

Incerti, D., Thom, H., Baio, G., & Jansen, J. P. (2019, May). R You Still Using Excel? The Advantages of Modern Software Tools for Health Technology Assessment. *Value in Health*, *22*(5), 575–579. Retrieved 2024-03-11, from https://www.sciencedirect.com/science/article/pii/S1098301519300506 doi: 10.1016/j.jval.2019.01.003

Ioannidis, J. P. A. (2005, August). Why Most Published Research Findings Are False. *PLOS Medicine*, *2*(8), e124. Retrieved 2024-04-22, from https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0020124 doi: 10.1371/journal.pmed.0020124

Jansen, B. J. H., Gilissen, C., Roelofs, H., Schaap-Oziemlak, A., Veltman, J. A., Raymakers, R. A. P., … Adema, G. J. (2010, April). Functional differences between mesenchymal stem cell populations are reflected by their transcriptome. *Stem cells and development*, *19*(4), 481–490. doi: 10.1089/scd.2009.0288

Jung, S.-H., & Lee, J.-J. (2022, April). Update on primary plasma cell leukemia. *Blood Research*, *57*(S1), 62–66. doi: 10.5045/br.2022.2022033

Kaplan, E. L., & Meier, P. (1958, June). Nonparametric Estimation from Incomplete Observations. *Journal of the American Statistical Association*, *53*(282), 457–481. Retrieved 2023-08-07, from http://www.tandfonline.com/doi/abs/10.1080/01621459.1958.10501452 doi: 10.1080/01621459.1958.10501452

Kastritis, E., Moulopoulos, L. A., Terpos, E., Koutoulidis, V., & Dimopoulos, M. A. (2014, December). The prognostic importance of the presence of more than one focal lesion in spine MRI of patients with asymptomatic (smoldering) multiple myeloma. *Leukemia*, *28*(12), 2402–2403. Retrieved 2024-05-23, from https://www.nature.com/articles/

leu2014230 doi: 10.1038/leu.2014.230

Katz, B.-Z. (2010, June). Adhesion molecules—The lifelines of multiple myeloma cells. *Seminars in Cancer Biology*, *20*(3), 186–195. Retrieved 2021-07-04, from https://linkinghub.elsevier.com/retrieve/pii/S1044579X10000246 doi: 10.1016/j.semcancer.2010.04.003

Kawano, M. M., Huang, N., Tanaka, H., Ishikawa, H., Sakai, A., Tanabe, O., … Kuramoto, A. (1991, December). Homotypic cell aggregations of human myeloma cells with ICAM-1 and LFA-1 molecules. *British Journal of Haematology*, *79*(4), 583–588. doi: 10.1111/j.1365-2141.1991.tb08085.x

Kazman, R., Bianco, P., Ivers, J., & Klein, J. (2020, December). *Maintainability* (Report). Carnegie Mellon University. Retrieved 2024-03-07, from https://kilthub.cmu.edu/articles/report/Maintainability/12954908/1 doi: 10.1184/R1/12954908.v1

Keats, J. J., Chesi, M., Egan, J. B., Garbitt, V. M., Palmer, S. E., Braggio, E., … Bergsagel, P. L. (2012, August). Clonal competition with alternating dominance in multiple myeloma. *Blood*, *120*(5), 1067–1076. doi: 10.1182/blood-2012-01-405985

Kelleher, R. (2024, January). *NVIDIA CEO: 'This Year, Every Industry Will Become a Technology Industry'.* Retrieved 2024-05-03, from https://blogs.nvidia.com/blog/nvidia-ceo-ai-drug-discovery-jp-morgan-healthcare-2024/

Kelly, B. S., Kirwan, A., Quinn, M. S., Kelly, A. M., Mathur, P., Lawlor, A., & Killeen, R. P. (2023, May). The ethical matrix as a method for involving people living with disease and the wider public (PPI) in near-term artificial intelligence research. *Radiography (London, England: 1995)*, *29 Suppl 1*, S103-S111. doi: 10.1016/j.radi.2023.03.009

Kibler, C., Schermutzki, F., Waller, H. D., Timpl, R., Müller, C. A., & Klein, G. (1998, June). Adhesive interactions of human multiple myeloma cell lines with different extracellular matrix molecules. *Cell Adhesion and Communication*, *5*(4), 307–323. doi: 10.3109/15419069809040300

Kim, D., Langmead, B., & Salzberg, S. L. (2015, April). HISAT: A fast spliced aligner with low memory requirements. *Nature methods*, *12*(4), 357–360. Retrieved 2024-04-26, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4655817/ doi: 10.1038/nmeth.3317

Kluyver, T., Ragan-Kelley, B., Pérez, F., Granger, B., Bussonnier, M., Frederic, J., … Jupyter Development Team (2016). *Jupyter Notebooks—a publishing format for reproducible computational workflows.* Retrieved 2024-04-20, from https://ui.adsabs.harvard.edu/abs/2016ppap.book...87K doi: 10.3233/978-1-61499-649-1-87

Krekel, H., Oliveira, B., Pfannschmidt, R., Bruynooghe, F., Laugher, B., & Bruhin, F. (2004). *Pytest.* Retrieved from https://github.com/pytest-dev/pytest

Krzywinski, M., & Savig, E. (2013, July). Multidimensional data. *Nature methods*, *10*(7), 595. Retrieved 2024-04-22, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6092027/

Kundu, S., Jha, S. B., Rivera, A. P., Flores Monar, G. V., Islam, H., Puttagunta, S. M., … Sange, I. (2022, February). Multiple Myeloma and Renal Failure: Mechanisms, Diagnosis, and Management. *Cureus*, *14*(2), e22585. Retrieved 2024-05-23, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8958144/ doi: 10.7759/cureus.22585

Kuric, M. (2024, April). *Markur4/plotastic.* Retrieved 2024-05-02, from https://github.com/markur4/plotastic

Kuric, M., Beck, S., Schneider, D., Rindt, W., Evers, M., Meißner-Weigl, J., … Ebert, R. (2024, April). Modeling Myeloma Dissemination In Vitro with hMSC-interacting Subpopulations of INA-6 Cells and Their Aggregation/Detachment Dynamics. *Cancer Research Communications*, *4*(4), 1150–1164. Retrieved 2024-05-14, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11057410/ doi: 10.1158/2767-9764.CRC-23-0411

Kuric, M., & Ebert, R. (2024, March). Plotastic: Bridging Plotting and Statistics in Python. *Journal of Open Source Software*, *9*(95), 6304. Retrieved 2024-03-11, from https://joss.theoj.org/papers/10.21105/joss.06304 doi: 10.21105/joss.06304

Kyle, R. A. (1997, February). Monoclonal gammopathy of undetermined significance and solitary plasmacytoma. Implications for progression to overt multiple myeloma. *Hematology/Oncology Clinics of North America*, *11*(1),

71–87. doi: 10.1016/s0889-8588(05)70416-0

Lai, T.-Y., Cao, J., Ou-Yang, P., Tsai, C.-Y., Lin, C.-W., Chen, C.-C., … Lee, C.-Y. (2022, April). Different methods of detaching adherent cells and their effects on the cell surface expression of Fas receptor and Fas ligand. *Scientific Reports*, *12*(1), 5713. Retrieved 2023-06-01, from https://www.nature.com/articles/s41598-022-09605-y doi: 10.1038/s41598-022-09605-y

Lakhlifi, C., Lejeune, F.-X., Rouault, M., Khamassi, M., & Rohaut, B. (2023, April). Illusion of knowledge in statistics among clinicians: Evaluating the alignment between objective accuracy and subjective confidence, an online survey. *Cognitive Research: Principles and Implications*, *8*, 23. Retrieved 2024-04-24, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10118231/ doi: 10.1186/s41235-023-00474-1

Leek, J. T., & Peng, R. D. (2015, April). Statistics: P values are just the tip of the iceberg. *Nature*, *520*(7549), 612–612. Retrieved 2024-04-22, from https://www.nature.com/articles/520612a doi: 10.1038/520612a

Li, H., Handsaker, B., Wysoker, A., Fennell, T., Ruan, J., Homer, N., … 1000 Genome Project Data Processing Subgroup (2009, August). The Sequence Alignment/Map format and SAMtools. *Bioinformatics*, *25*(16), 2078–2079. Retrieved 2023-06-09, from https://doi.org/10.1093/bioinformatics/btp352 doi: 10.1093/bioinformatics/btp352

Liu, Z., Liu, H., He, J., Lin, P., Tong, Q., & Yang, J. (2020, May). Myeloma cells shift osteoblastogenesis to adipogenesis by inhibiting the ubiquitin ligase MURF1 in mesenchymal stem cells. *Science signaling*, *13*(633), eaay8203. Retrieved 2024-06-08, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7376968/ doi: 10.1126/scisignal.aay8203

Localio, A. R., Goodman, S. N., Meibohm, A., Cornell, J. E., Stack, C. B., Ross, E. A., & Mulrow, C. D. (2018, June). Statistical Code to Support the Scientific Story. *Annals of Internal Medicine*, *168*(11), 828–829. Retrieved 2024-04-23, from https://www.acpjournals.org/doi/10.7326/M17-3431 doi: 10.7326/M17-3431

Love, M. I., Huber, W., & Anders, S. (2014, December). Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biology*, *15*(12), 550. Retrieved 2024-04-26, from https://doi.org/10.1186/s13059-014-0550-8 doi: 10.1186/s13059-014-0550-8

Mai, E. K., Hielscher, T., Kloth, J. K., Merz, M., Shah, S., Raab, M. S., … Hillengass, J. (2015, June). A magnetic resonance imaging-based prognostic scoring system to predict outcome in transplant-eligible patients with multiple myeloma. *Haematologica*, *100*(6), 818–825. Retrieved 2024-05-23, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4450628/ doi: 10.3324/haematol.2015.124115

Maichl, D. S., Kirner, J. A., Beck, S., Cheng, W.-H., Krug, M., Kuric, M., … Jundt, F. (2023, September). Identification of NOTCH-driven matrisome-associated genes as prognostic indicators of multiple myeloma patient survival. *Blood Cancer Journal*, *13*(1), 1–6. Retrieved 2023-09-05, from https://www.nature.com/articles/s41408-023-00907-6 doi: 10.1038/s41408-023-00907-6

Majithia, N., Rajkumar, SV., Lacy, MQ., Buadi, FK., Dispenzieri, A., Gertz, MA., … Kumar, SK. (2016, November). Early relapse following initial therapy for multiple myeloma predicts poor outcomes in the era of novel agents. *Leukemia*, *30*(11), 2208–2213. Retrieved 2022-10-15, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541860/ doi: 10.1038/leu.2016.147

Mangolini, M., & Ringshausen, I. (2020, February). Bone Marrow Stromal Cells Drive Key Hallmarks of B Cell Malignancies. *International Journal of Molecular Sciences*, *21*(4), 1466. Retrieved 2023-05-02, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7073037/ doi: 10.3390/ijms21041466

Manifesto for Agile Software Development. (2001). Retrieved 2024-05-14, from http://agilemanifesto.org/

Martin, S. K., Diamond, P., Williams, S. A., To, L. B., Peet, D. J., Fujii, N., … Zannettino, A. C. W. (2010, May). Hypoxia-inducible factor-2 is a novel regulator of aberrant CXCL12 expression in multiple myeloma plasma cells. *Haematologica*, *95*(5), 776–784. doi: 10.3324/haematol.2009.015628

Mateos María-Victoria, Hernández Miguel-Teodoro, Giraldo Pilar, de la Rubia Javier, de Arriba Felipe, Corral Lucía López, … San Miguel Jesús-F. (2013). Lenalidomide plus Dexamethasone for High-Risk Smoldering Multiple Myeloma. *New England Journal of Medicine*, *369*(5), 438–447. Retrieved 2024-05-22, from https://www.nejm.org/

doi/full/10.1056/NEJMoa1300439 doi: 10.1056/NEJMoa1300439

McCall, M. N., McMurray, H. R., Land, H., & Almudevar, A. (2014, August). On non-detects in qPCR data. *Bioinformatics*, *30*(16), 2310–2316. Retrieved 2023-04-25, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4133581/ doi: 10.1093/bioinformatics/btu239

McKay, B. S., Irving, P. E., Skumatz, C. M., & Burke, J. M. (1997, November). Cell-cell adhesion molecules and the development of an epithelial phenotype in cultured human retinal pigment epithelial cells. *Experimental Eye Research*, *65*(5), 661–671. doi: 10.1006/exer.1997.0374

McKinney, W. (2010, January). Data Structures for Statistical Computing in Python. In (pp. 56–61). doi: 10.25080/Majora-92bf1922-00a

Mckinney, W. (2011, January). Pandas: A Foundational Python Library for Data Analysis and Statistics. *Python High Performance Science Computer*.

Mesirov, J. P. (2010, January). Accessible Reproducible Research. *Science*, *327*(5964), 415–416. Retrieved 2024-04-22, from https://www.science.org/doi/10.1126/science.1179653 doi: 10.1126/science.1179653

Moleiro, A. F., Conceição, G., Leite-Moreira, A. F., & Rocha-Sousa, A. (2017). A Critical Analysis of the Available In Vitro and Ex Vivo Methods to Study Retinal Angiogenesis. *Journal of Ophthalmology*, *2017*, 3034953. doi: 10.1155/2017/3034953

Moñivas Gallego, E., & Zurita Castillo, M. (2024, April). Mesenchymal stem cell therapy in ischemic stroke trials. A systematic review. *Regenerative Therapy*, *27*, 301–306. Retrieved 2024-06-10, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11021793/ doi: 10.1016/j.reth.2024.03.026

Moran, M. (2003). Arguments for rejecting the sequential Bonferroni in ecological studies. *Oikos*, *100*(2), 403–405. Retrieved 2024-04-24, from https://onlinelibrary.wiley.com/doi/abs/10.1034/j.1600-0706.2003.12010.x doi: 10.1034/j.1600-0706.2003.12010.x

Morè, S., Corvatta, L., Manieri, V. M., Morsia, E., Poloni, A., & Offidani, M. (2023, November). Novel Immunotherapies and Combinations: The Future Landscape of Multiple Myeloma Treatment. *Pharmaceuticals*, *16*(11), 1628. Retrieved 2024-05-22, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10675193/ doi: 10.3390/ph16111628

Motulsky, H. (2018). *Intuitive Biostatistics: A Nonmathematical Guide to Statistical Thinking*. Oxford University Press.

Mrozik, K. M., Cheong, C. M., Hewett, D., Chow, A. W., Blaschuk, O. W., Zannettino, A. C., & Vandyke, K. (2015). Therapeutic targeting of N-cadherin is an effective treatment for multiple myeloma. *British Journal of Haematology*, *171*(3), 387–399. Retrieved 2024-05-26, from https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.13596 doi: 10.1111/bjh.13596

Muruganandan, S., Roman, A. A., & Sinal, C. J. (2009, January). Adipocyte differentiation of bone marrow-derived mesenchymal stem cells: Cross talk with the osteoblastogenic program. *Cellular and molecular life sciences : CMLS*, *66*(2), 236–253. doi: 10.1007/s00018-008-8429-z

Myers, G. J., Sandler, C., & Badgett, T. (2011). *The art of software testing* (3rd ed.). Wiley Publishing. Retrieved from https://malenezi.github.io/malenezi/SE401/Books/114-the-art-of-software-testing-3-edition.pdf

Narzt, W., Pichler, J., Pirklbauer, K., & Zwinz, M. (1998, January). A Reusability Concept for Process Automation Software..

Newville, M., Stensitzki, T., Allen, D. B., & Ingargiola, A. (2014, September). *LMFIT: Non-Linear Least-Square Minimization and Curve-Fitting for Python.* Zenodo. Retrieved 2023-05-30, from https://zenodo.org/record/11813 doi: 10.5281/zenodo.11813

Nilsson, K., Bennich, H., Johansson, S. G., & Pontén, J. (1970, October). Established immunoglobulin producing myeloma (IgE) and lymphoblastoid (IgG) cell lines from an IgE myeloma patient. *Clinical and Experimental Immunology*, *7*(4), 477–489.

Nowotschin, S., & Hadjantonakis, A.-K. (2010, August). Cellular dynamics in the early mouse embryo: From axis

formation to gastrulation. *Current opinion in genetics & development*, *20*(4), 420–427. doi: 10.1016/j.gde.2010.05.008

Oba, Y., Lee, J. W., Ehrlich, L. A., Chung, H. Y., Jelinek, D. F., Callander, N. S., … Roodman, G. D. (2005, March). MIP-1alpha utilizes both CCR1 and CCR5 to induce osteoclast formation and increase adhesion of myeloma cells to marrow stromal cells. *Experimental Hematology*, *33*(3), 272–278. doi: 10.1016/j.exphem.2004.11.015

Ocias, L. F., Larsen, T. S., Vestergaard, H., Friis, L. S., Abildgaard, N., Frederiksen, H., & Academy of Geriatric Cancer Research (AgeCare). (2016). Trends in hematological cancer in the elderly in Denmark, 1980-2012. *Acta Oncologica (Stockholm, Sweden)*, *55 Suppl 1*, 98–107. doi: 10.3109/0284186X.2015.1115124

O'Connor, B. P., Raman, V. S., Erickson, L. D., Cook, W. J., Weaver, L. K., Ahonen, C., … Noelle, R. J. (2004, January). BCMA Is Essential for the Survival of Long-lived Bone Marrow Plasma Cells. *The Journal of Experimental Medicine*, *199*(1), 91–98. Retrieved 2024-05-26, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1887725/ doi: 10.1084/jem.20031330

Okuno, Y., Takahashi, T., Suzuki, A., Ichiba, S., Nakamura, K., Okada, T., … Imura, H. (1991, February). In vitro growth pattern of myeloma cells in liquid suspension or semi-solid culture containing interleukin-6. *International Journal of Hematology*, *54*(1), 41–47.

Ordak, M. (2023, September). ChatGPT's Skills in Statistical Analysis Using the Example of Allergology: Do We Have Reason for Concern? *Healthcare (Basel, Switzerland)*, *11*(18), 2554. doi: 10.3390/healthcare11182554

Paiva, B., Paino, T., Sayagues, J.-M., Garayoa, M., San-Segundo, L., Martín, M., … San Miguel, J. F. (2013, November). Detailed characterization of multiple myeloma circulating tumor cells shows unique phenotypic, cytogenetic, functional, and circadian distribution profile. *Blood*, *122*(22), 3591–3598. doi: 10.1182/blood-2013-06-510453

Paiva, B., Pérez-Andrés, M., Vídriales, M.-B., Almeida, J., de las Heras, N., Mateos, M.-V., … Myeloma Stem Cell Network (MSCNET) (2011, April). Competition between clonal plasma cells and normal cells for potentially overlapping bone marrow niches is associated with a progressively altered cellular distribution in MGUS vs myeloma. *Leukemia*, *25*(4), 697–706. doi: 10.1038/leu.2010.320

Paszke, A., Gross, S., Massa, F., Lerer, A., Bradbury, J., Chanan, G., … Chintala, S. (2019, December). *PyTorch: An Imperative Style, High-Performance Deep Learning Library* (No. arXiv:1912.01703). arXiv. Retrieved 2024-03-07, from http://arxiv.org/abs/1912.01703 doi: 10.48550/arXiv.1912.01703

Peng, R. D. (2011, December). Reproducible Research in Computational Science. *Science*, *334*(6060), 1226–1227. Retrieved 2024-03-18, from https://www.science.org/doi/10.1126/science.1213847 doi: 10.1126/science.1213847

Perez, F., & Granger, B. E. (2007, May). IPython: A System for Interactive Scientific Computing. *Computing in Science & Engineering*, *9*(3), 21–29. Retrieved 2024-04-20, from https://ieeexplore.ieee.org/document/4160251 doi: 10.1109/MCSE.2007.53

Pérez-Andrés, M., Almeida, J., Martín-Ayuso, M., Moro, M. J., Martín-Nuñez, G., Galende, J., … Spanish Network of Cancer Research Centers (C03/10) (2005, March). Clonal plasma cells from monoclonal gammopathy of undetermined significance, multiple myeloma and plasma cell leukemia show different expression profiles of molecules involved in the interaction with the immunological bone marrow microenvironment. *Leukemia*, *19*(3), 449–455. doi: 10.1038/sj.leu.2403647

Perneger, T. V. (1998, April). What's wrong with Bonferroni adjustments. *BMJ : British Medical Journal*, *316*(7139), 1236–1238. Retrieved 2021-11-24, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1112991/

Pfaffl, M. W. (2001, May). A new mathematical model for relative quantification in real-time RT–PCR. *Nucleic Acids Research*, *29*(9), e45. Retrieved 2024-05-16, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC55695/

Pittenger, M. F., Mackay, A. M., Beck, S. C., Jaiswal, R. K., Douglas, R., Mosca, J. D., … Marshak, D. R. (1999). Multilineage Potential of Adult Human Mesenchymal Stem Cells. , *284*(April), 143–148. doi: 10.1126/science.284.5411.143

Podar, K., & Leleu, X. (2021, October). Relapsed/Refractory Multiple Myeloma in 2020/2021 and Beyond. *Cancers*,

13(20), 5154. Retrieved 2024-05-22, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8534171/ doi: 10.3390/cancers13205154

Polager, S., & Ginsberg, D. (2009, October). P53 and E2f: Partners in life and death. *Nature Reviews Cancer*, *9*(10), 738–748. Retrieved 2023-02-14, from https://www.nature.com/articles/nrc2718 doi: 10.1038/nrc2718

Purschke, M., Rubio, N., Held, K. D., & Redmond, R. W. (2010, November). Phototoxicity of Hoechst 33342 in time-lapse fluorescence microscopy. *Photochemical & Photobiological Sciences*, *9*(12), 1634–1639. Retrieved 2022-03-03, from https://pubs.rsc.org/en/content/articlelanding/2010/pp/c0pp00234h doi: 10.1039/C0PP00234H

PyMOL. (2024). Retrieved 2024-04-30, from https://pymol.org/

The Python Language Reference. (2024). Retrieved 2024-03-07, from https://docs.python.org/3/reference/index.html

Qasim, W., Zhan, H., Samarasinghe, S., Adams, S., Amrolia, P., Stafford, S., … Veys, P. (2017, January). Molecular remission of infant B-ALL after infusion of universal TALEN gene-edited CAR T cells. *Science Translational Medicine*, *9*(374), eaaj2013. doi: 10.1126/scitranslmed.aaj2013

Qiang, Y.-W., Barlogie, B., Rudikoff, S., & Shaughnessy, J. D. (2008, April). Dkk1-induced inhibition of Wnt signaling in osteoblast differentiation is an underlying mechanism of bone loss in multiple myeloma. *Bone*, *42*(4), 669–680. doi: 10.1016/j.bone.2007.12.006

Quanbeck, A., Hennessy, R. G., & Park, L. (2022, November). Applying concepts from "rapid" and "agile" implementation to advance implementation research. *Implementation Science Communications*, *3*(1), 118. doi: 10.1186/s43058-022-00366-3

Qureshi, R., Shaughnessy, D., Gill, K. A. R., Robinson, K. A., Li, T., & Agai, E. (2023, April). Are ChatGPT and large language models "the answer" to bringing us closer to systematic review automation? *Systematic Reviews*, *12*, 72. Retrieved 2024-05-03, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10148473/ doi: 10.1186/s13643-023-02243-z

R Core Team. (2018). *R: A language and environment for statistical computing* [Manual]. Vienna, Austria. Retrieved from https://www.R-project.org/

Radford, A., Wu, J., Child, R., Luan, D., Amodei, D., & Sutskever, I. (2019). Language Models are Unsupervised Multitask Learners.. Retrieved 2024-03-07, from https://www.semanticscholar.org/paper/Language-Models-are-Unsupervised-Multitask-Learners-Radford-Wu/9405cc0d6169988371b2755e573cc28650d14dfe

Rajkumar, S. V., Dimopoulos, M. A., Palumbo, A., Blade, J., Merlini, G., Mateos, M.-V., … Miguel, J. F. S. (2014, November). International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *The Lancet. Oncology*, *15*(12), e538-548. doi: 10.1016/S1470-2045(14)70442-5

Rajkumar, S. V., & Kumar, S. (2020, September). Multiple myeloma current treatment algorithms. *Blood Cancer Journal*, *10*(9), 94. Retrieved 2023-07-03, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7523011/ doi: 10.1038/s41408-020-00359-2

Ramakers, C., Ruijter, J. M., Deprez, R. H., & Moorman, A. F. (2003, March). Assumption-free analysis of quantitative real-time polymerase chain reaction (PCR) data. *Neuroscience Letters*, *339*(1), 62–66. Retrieved 2022-11-27, from https://linkinghub.elsevier.com/retrieve/pii/S0304394002014234 doi: 10.1016/S0304-3940(02)01423-4

Rayhan, A., & Gross, D. (2023). *The Rise of Python: A Survey of Recent Research.* doi: 10.13140/RG.2.2.27388.92809

Read the Docs. (2024). Retrieved 2024-05-03, from https://docs.readthedocs.io/en/stable/index.html

Rebl, H., Finke, B., Schroeder, K., & Nebe, J. B. (2010, October). Time-dependent metabolic activity and adhesion of human osteoblast-like cells on sensor chips with a plasma polymer nanolayer. *The International Journal of Artificial Organs*, *33*(10), 738–748.

Ribatti, D., Tamma, R., & Annese, T. (2020, June). Epithelial-Mesenchymal Transition in Cancer: A Historical Overview. *Translational Oncology*, *13*(6), 100773. doi: 10.1016/j.tranon.2020.100773

Rigsby, R. E., & Parker, A. B. (2016, September). Using the PyMOL application to reinforce visual understanding

of protein structure. *Biochemistry and Molecular Biology Education: A Bimonthly Publication of the International Union of Biochemistry and Molecular Biology*, *44*(5), 433–437. doi: 10.1002/bmb.20966

Robinson, M. D., McCarthy, D. J., & Smyth, G. K. (2010, January). edgeR: A Bioconductor package for differential expression analysis of digital gene expression data. *Bioinformatics (Oxford, England)*, *26*(1), 139–140. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19910308 doi: 10.1093/bioinformatics/btp616

Roy, P., Mukherjee, T., Chatterjee, B., Vijayaragavan, B., Banoth, B., & Basak, S. (2017, March). Non-canonical NFκB mutations reinforce pro-survival TNF response in multiple myeloma through an autoregulatory RelB:p50 NFκB pathway. *Oncogene*, *36*(10), 1417–1429. Retrieved 2024-06-08, from https://www.nature.com/articles/onc2016309 doi: 10.1038/onc.2016.309

Roy, P., Sarkar, U., & Basak, S. (2018, May). The NF-κB Activating Pathways in Multiple Myeloma. *Biomedicines*, *6*(2), 59. Retrieved 2021-07-25, from http://www.mdpi.com/2227-9059/6/2/59 doi: 10.3390/biomedicines6020059

Rueden, C. T., Schindelin, J., Hiner, M. C., DeZonia, B. E., Walter, A. E., Arena, E. T., & Eliceiri, K. W. (2017, November). ImageJ2: ImageJ for the next generation of scientific image data. *BMC Bioinformatics*, *18*(1), 529. Retrieved 2024-04-25, from https://doi.org/10.1186/s12859-017-1934-z doi: 10.1186/s12859-017-1934-z

Ruijter, J. M., Barnewall, R. J., Marsh, I. B., Szentirmay, A. N., Quinn, J. C., van Houdt, R., … van den Hoff, M. J. B. (2021, June). Efficiency Correction Is Required for Accurate Quantitative PCR Analysis and Reporting. *Clinical Chemistry*, *67*(6), 829–842. Retrieved 2023-05-27, from https://doi.org/10.1093/clinchem/hvab052 doi: 10.1093/clinchem/hvab052

Ruiz-Villalba, A., Ruijter, J. M., & van den Hoff, M. J. B. (2021, May). Use and Misuse of Cq in qPCR Data Analysis and Reporting. *Life*, *11*(6), 496. Retrieved 2023-04-25, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8229287/ doi: 10.3390/life11060496

Ruksakulpiwat, S., Kumar, A., & Ajibade, A. (2023, May). Using ChatGPT in Medical Research: Current Status and Future Directions. *Journal of Multidisciplinary Healthcare*, *16*, 1513–1520. Retrieved 2024-05-03, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10239248/ doi: 10.2147/JMDH.S413470

Sacchetti, B., Funari, A., Remoli, C., Giannicola, G., Kogler, G., Liedtke, S., … Bianco, P. (2016). No identical "mesenchymal stem cells" at different times and sites: Human committed progenitors of distinct origin and differentiation potential are incorporated as adventitial cells in microvessels. *Stem Cell Reports*, *6*(6), 897–913. Retrieved from http://dx.doi.org/10.1016/j.stemcr.2016.05.011 doi: 10.1016/j.stemcr.2016.05.011

Sandve, G. K., Nekrutenko, A., Taylor, J., & Hovig, E. (2013, October). Ten Simple Rules for Reproducible Computational Research. *PLoS Computational Biology*, *9*(10), e1003285. Retrieved 2024-03-07, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3812051/ doi: 10.1371/journal.pcbi.1003285

Santos, B. S., Silva, I., Ribeiro-Dantas, M. d. C., Alves, G., Endo, P. T., & Lima, L. (2020, October). COVID-19: A scholarly production dataset report for research analysis. *Data in Brief*, *32*, 106178. doi: 10.1016/j.dib.2020.106178

Sanz-Rodríguez, F., Ruiz-Velasco, N., Pascual-Salcedo, D., & Teixidó, J. (1999, December). Characterization of VLA-4-dependent myeloma cell adhesion to fibronectin and VCAM-1: VLA-4-dependent Myeloma Cell Adhesion. *British Journal of Haematology*, *107*(4), 825–834. Retrieved 2023-04-02, from http://doi.wiley.com/10.1046/j.1365-2141.1999.01762.x doi: 10.1046/j.1365-2141.1999.01762.x

Sarin, V., Yu, K., Ferguson, I. D., Gugliemini, O., Nix, M. A., Hann, B., … Wiita, A. P. (2020, October). Evaluating the efficacy of multiple myeloma cell lines as models for patient tumors via transcriptomic correlation analysis. *Leukemia*, *34*(10), 2754–2765. doi: 10.1038/s41375-020-0785-1

Seabold, S., & Perktold, J. (2010). Statsmodels: Econometric and Statistical Modeling with Python. In *Python in Science Conference* (pp. 92–96). Austin, Texas. Retrieved 2023-05-29, from https://conference.scipy.org/proceedings/scipy2010/seabold.html doi: 10.25080/Majora-92bf1922-011

Seckinger, A., Delgado, J. A., Moser, S., Moreno, L., Neuber, B., Grab, A., … Vu, M. D. (2017, March). Target Expression, Generation, Preclinical Activity, and Pharmacokinetics of the BCMA-T Cell Bispecific Antibody EM801

for Multiple Myeloma Treatment. *Cancer Cell*, *31*(3), 396–410. Retrieved 2023-07-21, from https://www.cell.com/cancer-cell/abstract/S1535-6108(17)30016-8 doi: 10.1016/j.ccell.2017.02.002

Seckinger, A., Hillengass, J., Emde, M., Beck, S., Kimmich, C., Dittrich, T., … Hose, D. (2018). CD38 as Immunotherapeutic Target in Light Chain Amyloidosis and Multiple Myeloma-Association With Molecular Entities, Risk, Survival, and Mechanisms of Upfront Resistance. *Frontiers in Immunology*, *9*, 1676. doi: 10.3389/fimmu.2018.01676

Shenghui, H., Nakada, D., & Morrison, S. J. (2009). Mechanisms of Stem Cell Self-Renewal. *Annual Review of Cell and Developmental Biology*, *25*(1), 377–406. Retrieved from https://doi.org/10.1146/annurev.cellbio.042308.113248 doi: 10.1146/annurev.cellbio.042308.113248

Sherina, V. (2020). Multiple imputation and direct estimation for qPCR data with non-detects.

Siclari, V., Guise, T., & Chirgwin, J. (2007, January). Molecular interactions between breast cancer cells and the bone microenvironment drive skeletal metastases. *Cancer metastasis reviews*, *25*, 621–33. doi: 10.1007/s10555-006-9023-1

Siegel, R. L., Giaquinto, A. N., & Jemal, A. (2024). Cancer statistics, 2024. *CA: A Cancer Journal for Clinicians*, *74*(1), 12–49. Retrieved 2024-05-21, from https://onlinelibrary.wiley.com/doi/abs/10.3322/caac.21820 doi: 10.3322/caac.21820

Smith, A. M., Niemeyer, K. E., Katz, D. S., Barba, L. A., Githinji, G., Gymrek, M., … Vanderplas, J. T. (2018). Journal of Open Source Software (JOSS): Design and first-year review. *PeerJ Preprints*, *4*, e147. doi: 10.7717/peerj-cs.147

Solimando, A. G., Malerba, E., Leone, P., Prete, M., Terragna, C., Cavo, M., & Racanelli, V. (2022, September). Drug resistance in multiple myeloma: Soldiers and weapons in the bone marrow niche. *Frontiers in Oncology*, *12*, 973836. Retrieved 2022-10-23, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9533079/ doi: 10.3389/fonc.2022.973836

Sphinx. (2024). Retrieved 2024-05-03, from https://docs.readthedocs.io/en/stable/intro/getting-started-with-sphinx.html

Sprynski, A. C., Hose, D., Caillot, L., Rème, T., Shaughnessy, J. D., Barlogie, B., … Klein, B. (2009, May). The role of IGF-1 as a major growth factor for myeloma cell lines and the prognostic relevance of the expression of its receptor. *Blood*, *113*(19), 4614–4626. Retrieved 2023-06-29, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2691749/ doi: 10.1182/blood-2008-07-170464

Standal, T., Seidel, C., Plesner, T., Sanderson, R., Waage, A., Børset, M., & Sundan, A. (2002, November). Osteoprotegerin is bound, internalized, and degraded by multiple myeloma cells. *Blood*, *100*, 3002–7. doi: 10.1182/blood-2002-04-1190

Stock, P., Bruckner, S., Winkler, S., Dollinger, M. M., & Christ, B. (2014, April). Human bone marrow mesenchymal stem cell-derived hepatocytes improve the mouse liver after acute acetaminophen intoxication by preventing progress of injury. *International journal of molecular sciences*, *15*(4), 7004–7028. doi: 10.3390/ijms15047004

Sullivan, G. M., & Feinn, R. S. (2021, August). Facts and Fictions About Handling Multiple Comparisons. *Journal of Graduate Medical Education*, *13*(4), 457–460. Retrieved 2024-03-10, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8370375/ doi: 10.4300/JGME-D-21-00599.1

Tabolacci, C., De Martino, A., Mischiati, C., Feriotto, G., & Beninati, S. (2019, January). The Role of Tissue Transglutaminase in Cancer Cell Initiation, Survival and Progression. *Medical Sciences*, *7*(2), 19. Retrieved 2023-03-17, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6409630/ doi: 10.3390/medsci7020019

Tai, Y.-T., Li, X.-F., Breitkreutz, I., Song, W., Neri, P., Catley, L., … Anderson, K. C. (2006, July). Role of B-cell-activating factor in adhesion and growth of human multiple myeloma cells in the bone marrow microenvironment. *Cancer Research*, *66*(13), 6675–6682. doi: 10.1158/0008-5472.CAN-06-0190

Tam, P. P., & Beddington, R. S. (1987, January). The formation of mesodermal tissues in the mouse embryo during gastrulation and early organogenesis. *Development (Cambridge, England)*, *99*(1), 109–126.

Taskiran, I. I., Spanier, K. I., Dickmänken, H., Kempynck, N., Pančíková, A., Ekşi, E. C., … Aerts, S. (2024, February). Cell-type-directed design of synthetic enhancers. *Nature*, *626*(7997), 212–220. Retrieved 2024-04-21, from https://

www.nature.com/articles/s41586-023-06936-2 doi: 10.1038/s41586-023-06936-2

Team, T. P. D. (2020, February). *Pandas-dev/pandas: Pandas.* Zenodo. Retrieved from https://doi.org/10.5281/zenodo.3509134 doi: 10.5281/zenodo.3509134

Teoh, G., & Anderson, K. C. (1997, February). INTERACTION OF TUMOR AND HOST CELLS WITH ADHESION AND EXTRACELLULAR MATRIX MOLECULES IN THE DEVELOPMENT OF MULTIPLE MYELOMA. *Hematology/Oncology Clinics of North America*, *11*(1), 27–42. Retrieved 2021-01-29, from http://www.sciencedirect.com/science/article/pii/S0889858805704135 doi: 10.1016/S0889-8588(05)70413-5

Teramachi, J., Silbermann, R., Yang, P., Zhao, W., Mohammad, K. S., Guo, J., … Kurihara, N. (2016, February). Blocking the ZZ Domain of Sequestosome1/p62 Suppresses Myeloma Growth and Osteoclast Formation In Vitro and Induces Dramatic Bone Formation in Myeloma-Bearing Bones In Vivo. *Leukemia*, *30*(2), 390–398. Retrieved 2024-06-08, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4740189/ doi: 10.1038/leu.2015.229

Terpos, E., Migkou, M., Christoulas, D., Gavriatopoulou, M., Eleutherakis-Papaiakovou, E., Kanellias, N., … Dimopoulos, M. A. (2016, May). Increased circulating VCAM-1 correlates with advanced disease and poor survival in patients with multiple myeloma: Reduction by post-bortezomib and lenalidomide treatment. *Blood Cancer Journal*, *6*(5), e428. Retrieved 2021-02-03, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4916305/ doi: 10.1038/bcj.2016.37

Terpos, E., Ntanasis-Stathopoulos, I., Gavriatopoulou, M., & Dimopoulos, M. A. (2018, January). Pathogenesis of bone disease in multiple myeloma: From bench to bedside. *Blood Cancer Journal*, *8*(1), 7. doi: 10.1038/s41408-017-0037-4

Thompson, S., Dowrick, T., Ahmad, M., Xiao, G., Koo, B., Bonmati, E., … Clarkson, M. J. (2020, July). SciKit-Surgery: Compact libraries for surgical navigation. *International Journal of Computer Assisted Radiology and Surgery*, *15*(7), 1075–1084. doi: 10.1007/s11548-020-02180-5

Thumallapally, N., Meshref, A., Mousa, M., & Terjanian, T. (2017, January). Solitary plasmacytoma: Population-based analysis of survival trends and effect of various treatment modalities in the USA. *BMC Cancer*, *17*, 13. Retrieved 2024-05-21, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216567/ doi: 10.1186/s12885-016-3015-5

Trapnell, C., Roberts, A., Goff, L., Pertea, G., Kim, D., Kelley, D. R., … Pachter, L. (2012, March). Differential gene and transcript expression analysis of RNA-seq experiments with TopHat and Cufflinks. *Nature Protocols*, *7*(3), 562–578. doi: 10.1038/nprot.2012.016

Tsubaki, M., Seki, S., Takeda, T., Chihara, A., Arai, Y., Morii, Y., … Nishida, S. (2020, October). The HGF/Met/NF-κB Pathway Regulates RANKL Expression in Osteoblasts and Bone Marrow Stromal Cells. *International Journal of Molecular Sciences*, *21*(21), 7905. Retrieved 2024-06-08, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7663721/ doi: 10.3390/ijms21217905

Turesson, I., Bjorkholm, M., Blimark, C. H., Kristinsson, S., Velez, R., & Landgren, O. (2018, April). Rapidly changing myeloma epidemiology in the general population: Increased incidence, older patients, and longer survival. *European journal of haematology*, 10.1111/ejh.13083. Retrieved 2024-05-22, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6195866/ doi: 10.1111/ejh.13083

Two new interleukin-6 dependent plasma cell lines carrying a chromosomal abnormality involving the IL-6 gene locus.Abstract Two plasma cell lines, INA-6 and JK-6, have been initiated and continuously cultured from two patients with malignant plasma cell diseases. Both cell lines are EBNA negative and show morphological and immunophenotypical features of plasma cells. INA-6 expresses the CD39 and CDw75 antigens, JK-6 is strongty positive with CD38 and CD39 antibodies. By flow cytometry they were non-reactive with Ia antibodies and B ceil reagents CD19, CD20, CD21, CD22, and CD24. While INA-6 cells are releasing kappa light chains only, JK-6 cells produce IgG kappa. Both cell lines could only be initiated with IL-6 supplemented medium and remained IL-6 responsive throughout continuous culture. INA-6 is strictly dependent on IL-6. No spontaneously secreted IL-6 was found nor could it be induced by IL-1beta /TNFalpha stimulation. Molecular analysis with RT-PCR revealed mRNA for the IL-6 receptor in both lines. No IL-6 mRNA was detectable in INA-6 cells, while in JK-6 minute amounts were observed.

Cytogenetic analysis of both lines revealed, among other abnormalities, a deletion (7)(p13). lnterestingly, the 7p deletion affects the location ot the IL-6 gene. ln both cell lines, IL-6 dependent proliferation could be inhibited by IFNalpha. IFNalpha had growth regulatory effects only on JK-6: While high concentrations were inhibitory, low IFNalpha amounts were clearly stimulatory. A wide variety of other cytokines including GM-CSF and IL-11 did not have the capacity to influence proliferation. These plasma cell lines do not only allow to turther characterize regulatory events in plasma cell neoplasias but also provide tools to study therapeutic interventions. (n.d.). Retrieved 2023-03-22, from https://www.cellosaurus.org/cellopub/CLPUB00060

Ullah, I., Subbarao, R. B., & Rho, G. J. (2015). Human mesenchymal stem cells - current trends and future prospective Bioscience Reports.
doi: 10.1042/BSR20150025

Urashima, M., Chauhan, D., Uchiyama, H., Freeman, G., & Anderson, K. (1995, April). CD40 ligand triggered interleukin-6 secretion in multiple myeloma. *Blood*, *85*(7), 1903–1912. Retrieved 2021-02-01, from https://ashpublications.org/blood/article/85/7/1903/123565/CD40-ligand-triggered-interleukin6-secretion-in doi: 10.1182/blood.V85.7.1903.bloodjournal8571903

Väänänen, H. K. (1993, August). Mechanism of bone turnover. *Annals of Medicine*, *25*(4), 353–359. doi: 10.3109/07853899309147297

Vallat, R. (2018, November). Pingouin: Statistics in Python. *Journal of Open Source Software*, *3*(31), 1026. Retrieved 2023-05-29, from https://joss.theoj.org/papers/10.21105/joss.01026 doi: 10.21105/joss.01026

van Rossum, G., Lehtosalo, J., & Langa, L. (2014). *PEP 484 – Type Hints | peps.python.org.* Retrieved 2024-03-08, from https://peps.python.org/pep-0484/

Vande Broek, I., Vanderkerken, K., Van Camp, B., & Van Riet, I. (2008). Extravasation and homing mechanisms in multiple myeloma. *Clinical & Experimental Metastasis*, *25*(4), 325–334. doi: 10.1007/s10585-007-9108-4

Van Valckenborgh, E., Croucher, P. I., De Raeve, H., Carron, C., De Leenheer, E., Blacher, S., … Vanderkerken, K. (2004, September). Multifunctional role of matrix metalloproteinases in multiple myeloma: A study in the 5T2MM mouse model. *The American Journal of Pathology*, *165*(3), 869–878. doi: 10.1016/S0002-9440(10)63349-4

Wadgaonkar, R., Phelps, K. M., Haque, Z., Williams, A. J., Silverman, E. S., & Collins, T. (1999, January). CREB-binding protein is a nuclear integrator of nuclear factor-kappaB and p53 signaling. *The Journal of Biological Chemistry*, *274*(4), 1879–1882. doi: 10.1074/jbc.274.4.1879

Wang, W., Yang, X., Dai, J., Lu, Y., Zhang, J., & Keller, E. T. (2019, June). Prostate cancer promotes a vicious cycle of bone metastasis progression through inducing osteocytes to secrete GDF15 that stimulates prostate cancer growth and invasion. *Oncogene*, *38*(23), 4540–4559. doi: 10.1038/s41388-019-0736-3

Waskom, M. L. (2021, April). Seaborn: Statistical data visualization. *Journal of Open Source Software*, *6*(60), 3021. Retrieved 2023-03-26, from https://joss.theoj.org/papers/10.21105/joss.03021 doi: 10.21105/joss.03021

Webster, G. A., & Perkins, N. D. (1999, May). Transcriptional Cross Talk between NF-κB and p53. *Molecular and Cellular Biology*, *19*(5), 3485–3495. Retrieved 2023-07-04, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC84141/

Weetall, M., Hugo, R., Maida, S., West, S., Wattanasin, S., Bouhel, R., … Friedman, C. (2001, June). A Homogeneous Fluorometric Assay for Measuring Cell Adhesion to Immobilized Ligand Using V-Well Microtiter Plates. *Analytical Biochemistry*, *293*(2), 277–287. Retrieved 2022-09-25, from https://linkinghub.elsevier.com/retrieve/pii/S0003269701951401 doi: 10.1006/abio.2001.5140

Weiss, C. J. (2022, September). Visualizing protein big data using Python and Jupyter notebooks. *Biochemistry and Molecular Biology Education: A Bimonthly Publication of the International Union of Biochemistry and Molecular Biology*, *50*(5), 431–436. doi: 10.1002/bmb.21621

West, K. (2018, July). *Reinventing Research: Agile in the Academic Laboratory | Agile Alliance.* Retrieved 2024-05-14, from https://www.agilealliance.org/resources/experience-reports/reinventing-research-agile-in-the

-academic-laboratory/

Wickham, H. (2014, September). Tidy Data. *Journal of Statistical Software*, *59*, 1–23. Retrieved 2023-11-15, from https://doi.org/10.18637/jss.v059.i10 doi: 10.18637/jss.v059.i10

Wilkins, A., Kemp, K., Ginty, M., Hares, K., Mallam, E., & Scolding, N. (2009, July). Human bone marrow-derived mesenchymal stem cells secrete brain-derived neurotrophic factor which promotes neuronal survival in vitro. *Stem cell research*, *3*(1), 63–70. doi: 10.1016/j.scr.2009.02.006

Wilkinson, M. D., Dumontier, M., Aalbersberg, I. J., Appleton, G., Axton, M., Baak, A., … Mons, B. (2016, March). The FAIR Guiding Principles for scientific data management and stewardship. *Scientific Data*, *3*(1), 160018. Retrieved 2024-03-18, from https://www.nature.com/articles/sdata201618 doi: 10.1038/sdata.2016.18

Witwer, K. W. (2013, February). Data submission and quality in microarray-based microRNA profiling. *Clinical chemistry*, *59*(2), 392–400. Retrieved 2024-04-22, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4037921/ doi: 10.1373/clinchem.2012.193813

Wong, A. D., & Searson, P. C. (2017, November). Mitosis-mediated intravasation in a tissue-engineered tumor-microvessel platform. *Cancer research*, *77*(22), 6453–6461. Retrieved 2023-07-14, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5690825/ doi: 10.1158/0008-5472.CAN-16-3279

Xu, W., Zhang, X., Qian, H., Zhu, W., Sun, X., Hu, J., … Chen, Y. (2004, July). Mesenchymal stem cells from adult human bone marrow differentiate into a cardiomyocyte phenotype in vitro. *Experimental biology and medicine (Maywood, N.J.)*, *229*(7), 623–631.

Yang, A., Troup, M., & Ho, J. W. (2017, July). Scalability and Validation of Big Data Bioinformatics Software. *Computational and Structural Biotechnology Journal*, *15*, 379–386. Retrieved 2024-03-07, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5537105/ doi: 10.1016/j.csbj.2017.07.002

Yang, P., Qu, Y., Wang, M., Chu, B., Chen, W., Zheng, Y., … Qian, Z. (2022, June). Pathogenesis and treatment of multiple myeloma. *MedComm*, *3*(2), e146. Retrieved 2024-05-21, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9162151/ doi: 10.1002/mco2.146

Yang, Y., Macleod, V., Bendre, M., Huang, Y., Theus, A. M., Miao, H.-Q., … Sanderson, R. D. (2005, February). Heparanase promotes the spontaneous metastasis of myeloma cells to bone. *Blood*, *105*(3), 1303–1309. doi: 10.1182/blood-2004-06-2141

Zeissig, M. N., Zannettino, A. C. W., & Vandyke, K. (2020, December). Tumour Dissemination in Multiple Myeloma Disease Progression and Relapse: A Potential Therapeutic Target in High-Risk Myeloma. *Cancers*, *12*(12). Retrieved 2021-02-03, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7761917/ doi: 10.3390/cancers12123643

Zerbino, D. R., Achuthan, P., Akanni, W., Amode, M. R., Barrell, D., Bhai, J., … Flicek, P. (2018, January). Ensembl 2018. *Nucleic Acids Research*, *46*(D1), D754-D761. Retrieved 2023-05-27, from https://doi.org/10.1093/nar/gkx1098 doi: 10.1093/nar/gkx1098

Zhou, F., Meng, S., Song, H., & Claret, F. X. (2013, November). Dickkopf-1 is a key regulator of myeloma bone disease: Opportunities and challenges for therapeutic intervention. *Blood reviews*, *27*(6), 261–267. Retrieved 2023-02-18, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4133945/ doi: 10.1016/j.blre.2013.08.002

Zhou, Y., Zhou, B., Pache, L., Chang, M., Khodabakhshi, A. H., Tanaseichuk, O., … Chanda, S. K. (2019, April). Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nature Communications*, *10*(1), 1523. Retrieved 2023-02-09, from https://www.nature.com/articles/s41467-019-09234-6 doi: 10.1038/s41467-019-09234-6

Ziemann, M., Eren, Y., & El-Osta, A. (2016, August). Gene name errors are widespread in the scientific literature. *Genome Biology*, *17*(1), 177. Retrieved 2024-04-30, from https://doi.org/10.1186/s13059-016-1044-7 doi: 10.1186/s13059-016-1044-7

Appendices

A Supplementary Data & Methods

A.1 Figures

?

A.2 Tables

A.3 Materials & Methods

B Documentation of plotastic