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# 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<sup>1</sup> 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 (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 MM* (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<sup>2</sup> (Abdallah et al., 2024; Mateos María-Victoria et al., 2013). MM itself can progress to advanced stages, such as *extramedullary involvement/disease*

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<sup>1</sup>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.*”

<sup>2</sup>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 patients, 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).

(EMD) 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 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 survival rate of 50 % (Turesson et al., 2018), MM can be considered incurable and deadly. MM relapses within the first year in 16 % of patients, 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 intracлонаl genetic heterogeneity within the myeloma cell population and the protective niche provided by the bone marrow microenvironment (Solimando et al., 2022).

## Dissemination of Myeloma Cells

As the name suggests, multiple myeloma (MM) 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 bone marrow (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 (Forster & Radpour, 2022).

Dissemination in multiple myeloma (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 to mesenchymal transition*, 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 mechanisms of MM dissemination are still not entirely understood. Nevertheless, attempts to structure this process have been made by Zeissig et al. (2020), describing MM dissemination in five-steps: *Retention in the BM environment (BME)*, *release from the BME*, *intravasation*, *extravasation*, and *colonization*. Critical to these processes is overcoming retention and adhesion within the BME, despite their dependency on the BM for survival factors.

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*. In the BM they can *colonize* and form new tumor foci. This complex interplay of cell signaling, adhesion, and the microenvironmental conditions not only dictates the dissemination paths of MM cells but also influences their survival and proliferation in new niches (Zeissig et al., 2020).

## Retention of Myeloma Cells in the Bone Marrow

According to Zeissig et al. (2020), the retention of MM cells within the BME is mediated by multiple mechanisms. Here, we categorise retention into *Direct adhesion*, *soluble survival factors* and *chemotaxis*. Another notable mechanism is the physical boundary that is bone tissue and extracellular matrix (ECM).

*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 mesenchymal stromal cells (BMSCs) (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). BM mesenchymal stromal cells (BMSCs) are vital in this niche, supporting cell adhesion through cell adhesion molecules (CAMs) but also by secretion of extracellular matrix (ECM) components (Katz, 2010). Such adhesion acts both as physical anchorage but also provides signaling cues for growth, survival, and drug resistance, a classic example being the binding of MM cell integrins, such as  $\alpha 4 \beta 1$  (VLA-4) to VCAM-1 on BMSCs, (Bou Zerdan et al., 2022).

*Soluble survival factors* contribute to BM retention, since plasma cells can not survive outside the bone marrow without them. These signals are secreted by the bone marrow MSCs and

adipocytes (Kibler et al., 1998; García-Ortiz et al., 2021).

IGF-1 has proven to be the primary survival factors (Sprynski et al., 2009)

like IL-6 and IGF-1 are essential to plasma cell survival and are solely present in the BME, being secreted by BMSCs and other BM cells (Sprynski et al., 2009)

*Chemotaxis* is also crucial for BM retention. CXCL12 and CXCL8 produced by BMSCs attract MM cells and prime their cytoskeleton and integrins for adhesion (Aggarwal et al., 2006; Alsayed et al., 2007).

## Release of Myeloma Cells from the Bone Marrow

Zeissig et al. (2020) describes the release of myeloma cells from the BME as all steps required for overcoming bone marrow retention. To the author’s knowledge, this step is the least understood within the dissemination process. However, Zeissig et al. (2020) outlays many interesting

MM cells must become partially independent from essential survival factors

. While the specific microenvironmental stimuli regulating this release are not fully defined, changes in the expression of adhesion molecules play a role. For example, circulating MM cells show lower levels of integrin  $\alpha4\beta1$  compared to those residing in the BM. Furthermore, treatment with a syndecan-1 blocking antibody has been shown to rapidly induce the mobilization of MM cells from the BM to peripheral blood in mouse models, suggesting that alterations in adhesion molecule expression facilitate MM cell release (Zeissig et al., 2020).

Loss of adhesion factors such as CD138 could be significant in this context (Akhmetzyanova et al., 2020; Brandl et al., 2022).

Notably, active degradation of bone tissue removes physical boundaries for MM cells, allowing them to disseminate to other sites.

This process is driven by a “vicious cycle” that maximizes bone destruction by extracting growth factors (EGF and TGF- ) stored in calcified tissues.

The hypoxic conditions within the BM during MM growth also influence cell release. Hypoxia induces changes in MM cell adherence to BMSCs and collagen, which may facilitate their release from the BM niche. Hypoxia-induced factors like HIF-2 can decrease MM cell responsiveness to stromal-derived CXCL12, thereby disrupting the CXCR4/CXCL12 retention signal and facilitating MM cell release (Zeissig et al., 2020).

## hMSCs: Human Mesenchymal Stromal/Stem Cells

The previous sections mentioned hMSCs several times, being a critical component of the bone marrow microenvironment (BME) in the context of multiple myeloma (Mangolini & Ringshausen, 2020). Before discussing their role in MM specifically, it is important to understand what hMSCs are.

Explaining what a mesenchymal stromal cell (MSC) is, can be challenging. MSCs are derived from multiple different sources, serve a wide array of functions and are always isolated as a heterogeneous 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.

hMSCs 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, producing another stem cell and a differentiated 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. Especially human mesenchymal stromal cells (hMSCs) have proven to be a promising candidate in this context (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. hMSCs 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, hMSCs can differ greatly in their transcription profile and *in vivo* differentiation potential (Jansen et al., 2010; Sacchetti et al., 2016).

Since hMSCs 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, hMSCs 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, hMSCs must differentiate to osteoblasts, adipocytes and chondroblasts *in vitro*. Together, hMSCs exhibit diverse differentiation potentials and can be isolated from multiple sources of the body.

## hMSC–Myeloma Interactions

As mentioned in previous sections MSCs are key drivers of MM pathology through mediating retention and survival of MM cells in the bone marrow (Mangolini & Ringshausen, 2020). Here, we outlay details of such interactions and present further mechanisms how interactions between MM and hMSC contribute to MM progression.

bone marrow microenvironment

it plays a

myeloma bone disease.

Bone is a two-phase system in which the mineral phase provides the stiffness and the collagen fibers provide the ductility and ability to absorb energy (Viguet-Carrin et al., 2006). On a molecular level, bone tissue is composed of extracellular matrix (ECM) proteins that are calcified by hydroxyapatite crystals. This ECM consists mostly of collagen type I, but also components with major regulatory activity, such as fibronectin and proteoglycans that are essential for healthy bone physiology (Alcorta-Sevillano et al., 2020). Bone tissue is actively remodeled by bone-forming osteoblasts and bone-degrading osteoclasts. Osteoblasts are derived from mesenchymal stromal cells (MSCs) that reside in the bone marrow (A. J. Friedenstein et al., 1966; Pittenger et al., 1999). MSCs also give rise to adipocytes (ACs) to form Bone Marrow Adipose

Tissue (BMAT), which can account for up to 70% of bone marrow volume (Fazeli et al., 2013).

MM indirectly degrades bone tissue by stimulating osteoclasts and inhibiting osteoblast differentiation, which leads to MM-related bone disease (MBD) (Glavey et al., 2017). MBD is present in 80% of patients at diagnosis and is characterized by osteolytic lesions, osteopenia and pathological fractures (Terpos et al., 2018).

from (Forster & Radpour, 2022):

# 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
- 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
- Alcorta-Sevillano, N., Macías, I., Infante, A., & Rodríguez, C. I. (2020, December). Deciphering the Relevance of Bone ECM Signaling. *Cells*, 9(12), 2630. Retrieved 2023-12-20, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7762413/> doi: 10.3390/cells9122630
- 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
- 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., Vaculčíaková, 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 CD138<sup>low</sup>/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). *Travis-md/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
- 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/imt.2.115
- 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
- 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., Adjero, 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>
- Fazeli, P. K., Horowitz, M. C., MacDougald, O. A., Scheller, E. L., Rodeheffer, M. S., Rosen, C. J., & Klibanski, A. (2013, March). Marrow Fat and Bone—New Perspectives. *The Journal of Clinical Endocrinology and Metabolism*, 98(3), 935–945. Retrieved 2023-12-20, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3590487/> doi: 10.1210/jc.2012-3634
- 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
- Fernand, 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.currprobcancer.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
- 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., Merckenschlager, 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>
- 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.semancer.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
- 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., Laughner, 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
- 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/>
- 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
- 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.
- 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
- 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
- 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
- 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
- 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. *Can-*

- cers*, 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
- 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
- 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](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.
- 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., Dickmanken, 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
- 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
- Turesson, I., Björkholm, 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 strongly positive with CD38 and CD39 antibodies. By flow cytometry they were non-reactive with Ia antibodies and B cell 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). Interestingly, the 7p deletion affects the location of the IL-6 gene. In 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 further 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
- 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/>
- Van Valkenborgh, 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
- Viguet-Carrin, S., Garnero, P., & Delmas, P. D. (2006, March). The role of collagen in bone strength. *Osteoporosis International*, 17(3), 319–336. Retrieved 2023-12-20, from <https://doi.org/10.1007/s00198-005-2035-9> doi: 10.1007/s00198-005-2035-9
- 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
- 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- $\kappa$ B 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
- 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`