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# Introduction

To provide a comprehensive background for the following chapters that focus on the interaction of human mesenchymal stromal cells (hMSCs) with multiple myeloma (MM) cells, this

## Aims

This project defines these aims:

- Characterize the interaction between myeloma cells and mesenchymal stromal cells
- Develop methods
- Face the challenge of time-dependent cell adhesion through
- Provide tools to analyze multidimensional cell adhesion data

## Summarising Discussion

### Time-Lapse Microscopy Added Intuition to Exploratory Cell Biology

- When starting this project, dissemination has not been the main topic. - Surprisingly, Time-lapse identified detaching cells - Hence, Time-lapse proved pivotal for this project, shifting the focus onto in vitro dissemination.

Microscopy holds vast amounts of information. Cell movements themselves add a lot more info. Time-lapse video has proven invaluable for exploratory cell biology

the most important key insight on the mechanism of dissemination identified by timelapse was Cell Division - further insights were multiple time measurements

measuring the minimum time for detachments to begin, or the time required for daughter cells to re-attach to the hMSC monolayer. Such mechanistic insights

Other methods like RNAseq and survival analysis did provide molecular and clinical connections, time-lapse microscopy documented cell interactions as-is, but allowed for a deep and intuitive understanding of cryptic molecular data, placing the conclusions into a context that answer key questions about potential and limits of this study, such as the aggregation behavior of INA-6 cells.

### Novel Methods of Isolating Adhering Subpopulations

cite all those methods for cell isolation! - Turning around wellplates: Doesn't allow isolation, just quantification - The author did not show all his washing experiments - Washing is very bad (data not shown): Highly dependent on user: position of cell on well bottom (border cells receive less force), position of pipette tip in well (depth, angle and position on bottom) - This motivated us to explore more reproducible methods

It's a challenge: either quantify cell population, or isolate them! - It's better to specialize in one method, than to do both poorly - Well Plate Sandwich Centrifugation is badly suited for quantification, but possible - we switched to developing V-well adhesion assay for quantification - We realized, V-well isolation allows both ultra precise quantification and isolation of small

amounts of cells! - unmatched precision through centrifugation, no washing - But V-well pellets comprise only few cells requiring a lot of technical replicates and an untiring pipetting hand

The Well Plate Sandwich Centrifugation (WPSC) used two different techniques to dissociate MA-INA6 cells from the hMSC monolayer. This had no impact on the ratio of isolated MA-INA6 to nMA-INA6, since nMA-INA6 isolation was performed prior to dissociation using the same protocol consistently. We tried this to test if MACS was really necessary, after all it is costly, time-consuming, introduces an antibody bias and requires cell cold-treatment during antibody: Strong pipetting (‘*Wash*’) and repeated Accutase treatment followed by magnetic activated cell sorting (‘*MACS*’).

## Outlook: High-Value Research Topics for Myeloma Research

As an Outlook, the Author lists research topics arising from this work that have great potential for breakthroughs in myeloma research.

**Cell Division as a Mechanism for Dissemination Initiation:** The author describes how the detachment of daughter cells from the mother cell after a cycle of hMSC-(re)attachment and proliferation could be a key mechanism in myeloma dissemination. This mechanism was shown in other studies of extravasation. The author sees great potential in this mechanism as a target for future research. It is probably under-researched due to requirement of sophisticated time-lapse equipment, yet the simplicity of detachment through cell division is intriguing through its simplicity. It implies asymmetric cell division. Cancer cells are known to divide asymmetrically, e.g. moving miRNAs to one daughter cell.

**Time as a Key Parameter:** The area Thermodynamics of started with scientists measuring how long it takes for gases to cool down. The author claims, by measuring the time it takes for cancer cells to detach could lead to breakthroughs in research of myeloma dissemination.

- Cell adhesion is highly time-dependent. - Cell detachment is required for metastasis and dissemination -

key mechanistic insights

measuring the minimum time for detachments to begin, or the time required for daughter cells to re-attach to the hMSC monolayer. Such mechanistic insights

The author recommends high time resolutions, e.g. 1 frame every 15 min, which is a high resolution for common live cell imaging when compared to Purschke et al. (2010). Time-resolution was mostly limited by available disk space. Investing into more hard drives is worth it, since

**Lists of Adhesion Gene Associated With Prolonged Patient Survival:** The author lists adhesion genes that are associated with prolonged patient survival. These genes are highly

expressed in myeloma samples from patients with longer overall

## Semi-Automated Analysis was Required for Establishing Methods

In this work, the development and publication of innovative *in vitro* methodologies (Well Plate Sandwich Centrifugation and V-Well adhesion Assay) necessitated the adoption of semi-automated data analysis tools. These novel methods introduced complexities that span multiple experimental parameters, making the results multidimensional. This demanded precise, efficient and standardized data handling capabilities which were facilitated by tools like `plotastic`.

**Inherent Multidimensionality of Adhesion Studies:** Cell adhesion studies often involve multiple independent parameters, posing significant analytical challenges. Two critical dimensions are particularly notable: ‘*Subpopulation*’ and ‘*Time*’. Analyzing cell adhesion often involves isolation of adherent and non-adherent subpopulations, effectively introducing ‘*Subpopulation*’ as a vital dimension in the dataset (Dziadowicz et al., 2022). This study specifically categorized cells into three levels of MSC-interaction: CM-INA6, nMA-INA6, and MA-INA6. Furthermore, the dynamic nature of cell adhesion processes is profoundly influenced by the factor ‘*Time*’, making it a crucial experimental parameter for investigation (Rebl et al., 2010; McKay et al., 1997; Bolado-Carrancio et al., 2020). This work includes extensive time-lapse microscopy experiments utilizing a high time resolution (1 frame every 15 min), similar to those time resolutions used by Purschke et al. (2010). This precision was required for key mechanistic insights on hMSC-INA-6 interaction dynamics. These included identifying rolling movements of nMA-INA6 daughter cells around MA-INA6 mother cells, measuring the minimum time for INA-6 detachments to begin, and measuring the time required for daughter cells to re-attach to the hMSC monolayer, etc. Next to mechanistic insights, adhesion time played a crucial methodological role in this study as well: During the V-Well adhesion experiments, we did not know initially how long INA-6 cells required to form strong adhesion with hMSCs before pelleting nMA-INA6, but required a timepoint with hour precision to capture detachments after cell division that was accelerated through prior cell cycle synchronization at M-Phase.

The extensive facetting features of `seaborn` and `plotastic` were essential for visualizing these multidimensional datasets, allowing for quick exploration of the data (Waskom, 2021).

**Further Contributions and Remedies to Multidimensional Complexity:** In addition to ‘*Subpopulation*’ and ‘*Time*’, this study faced additional layers of complexity that were managed through semi-automated analysis.

Experiments typically involved at least three biological replicates and corresponding technical replicates. Although replicates were not treated as independent variables – instead serving for displaying variance – they can add substantially to the data management workload. In this

work, semi-automation nullified the manual burdens of handling replicates: pandas was used to automate aggregation of technical replicates into means after removing technical outliers thorough z-score thresholding, while the jupyter notebook format allowed for reviewing filtered data for specific data losses. The removal of technical noise was especially relevant for qPCR data, where low gene expression can lead to sudden increase in Ct value (non-detects). In fact, the decision to remove or impute non-detects is under active discussion, however, available algorithms are hard to understand for non bioinformaticians, but also do not separate biological from technical variance, which is considered bad practice by Motulsky (2018) (McCall et al., 2014; Sherina, 2020). Semi-automation also nullified the burden of handling biological replicates: The automatic aggregation of datapoints during plotting is a key feature of seaborn, on which plotastic was built. Without such automation, calculating means and standard deviations for simple barplots would have required extensive manual computation in *Microsoft Excel*, or tedious plot configurations in *Graphpad Prism* due to limited facetting functionality of multiple variable tables (*GraphPad Prism 10 User Guide*, 2024).

Replicates can expand datasets as this factor comprises a lot of levels. Similarly, the factor ‘Gene’ multiplied the dataset by a total of 30 genes when validating RNAseq data with RT-qPCR. With three subpopulations, one timepoint, eleven biological replicates, and three technical replicates, the qPCR dataset used in this study grew to 2970 datapoints to be statistically analyzed and visualized. This is a manageable size for manual analysis, but the effort involved illustrates the definition of semi-big data.

Methodological variability also introduced additional dimensions: The Well Plate Sandwich Centrifugation (WPSC) used two different techniques to dissociate MA-INA6 cells from the hMSC monolayer: Strong pipetting (‘Wash’) and repeated Accutase treatment followed by magnetic activated cell sorting (‘MACS’). These variations, recorded as the factor ‘method’, further complicated the dataset. Although this distinction is not discussed in this work – rather pooled into one group –, this showcases how protocol changes can add dimensions to the dataset that are not necessarily relevant for the biological question but essential for method optimizations and validation.

**Agility During Establishment of V-Well Assay** - What is agility in laboratory? Cite the agile manifesto? - The last part of the agile manifesto of software Development states ‘Responding to change over following a plan’ (*Manifesto for Agile Software Development*, 2001). This idea has also gained attraction in biomedical research (West, 2018). This is especially true for the establishment of new methods in the laboratory.

Was plotastic useful for me? - Yes incredibly. I was able to perform the statistical tests and visualize the data in a fraction of the time that I would have needed manually. This allowed me to focus on the interpretation of the results and the writing of the manuscript. There was



one particular example during establishing the V-Well adhesion assay, where my analysis was so fast, that I fed raw datatables during microscopy into python scripts and was able to adapt the experimental technique during the experiment. This allows for an agile and adaptive work environment that is not possible with manual analysis and proved invaluable during development of *in vitro* methods.

seaborn proved invaluable to cell cycle profiling: Plotting figure ?? which is

Further research is needed to assess the true impact of semi-automated analysis on the agility of establishing new *in vitro* methods.

### **Quick Exploration and (Re-)Analysis using plotastic**

- Was plotastic needed for quick data visualization Visualizations often times requires several attempts to find the best representation of the data. This is especially true for this study here that presents a new methodology for studying myeloma dissemination. This often times involves re-arranging which factors are represented on the x-axis or are color-coded. seaborn already works fine with experimentation by easy changes to faceting, plotastic extends the functionality of seaborn with the `.switch()` method. However, plotastic was mostly required for its multiplots feature to automate execution multiple seaborn functions with consistent plotting formats across the whole paper in order to display individual datapoints, which is a requirement for many journals.

- Re-analysis plotastic proved invaluable for re-arranging plots. With graphpad prism, this would have required re-annotating the plots, redoing most of the analysis pipeline manually every time a change was made.

However, when re-arranging factors, statistical annotations have to be redone as well. This is where plotastic shines, as it allows for easy re-analysis of the data, without the need to re-calculate the statistical tests and re-annotating them.

During the peer review process of Kuric et al. (2024), which was necessary for Figure ??. To the author's experience, common tools can cause frustration,

Given the complexity of planned examples, it is clear that a new tool had to be developed, and given the simplicity of plotastic.

For example, the reproducibility of qPCR has been a long-standing issue in the field <sup>5</sup>. These issues often refer to the analysis method of raw data. The author argues that sophisticated (re-) analysis are highly unattractive for average biomedical researchers, when facing semi-big data, since non-automated data handling does not leave time for applying newest data analysis techniques, let alone hinder a quick re-analysis of the data.

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<sup>5</sup>Bustin (2014): "*By 2009 it was pretty obvious that many publications using PCR based methods were seriously flawed* "

**Intermediate Conclusion:** Together, adhesion studies, especially combined with methodologies that further add dimensions (Cell Cycle profiling), explode experimental complexity, which require sophisticated tools for high requirements posed by multidimensionality

These requirements were facilitated by `seaborn` for quick processing of intermediate results during method optimizations and by `plotastic` for designing publication-grade analyses and figures. Developing `plotastic` was mostly a necessity that arose from late-stage data processing (statistics, and publication figures), filling `seaborn`'s shortcomings, but also ensured standards for consistent plot formatting and statistical analysis. The author lays emphasis on `plotastic` as an infrastructure for quick and confident re-structuring of publication figures that include statistical annotations, especially during his peer-review process.

## Challenges of Integrating `plotastic` into Biomedicine

Although `plotastic` is designed for the overall scientific community and has passed peer-review, time will tell if the single author's vision of an optimized automated statistical workflow can be extrapolated to biomedicine. The author's himself continues to use `plotastic` in future projects that require visualizing single datapoints and statistical rigor.

For biomedicine overall, the author sees the greatest challenge in adopting `plotastic` since it is a tool based on a command line interface (CLI), whereas the majority of biologists prefer graphical user interfaces (GUI). The author argues that a CLI can perform everything that a GUI can, but better, faster, and more efficiently, provided that one is willing to undergo the switch, which can be intimidating. However, many python tools already provide extremely easy commands (e.g. `seaborn`), and `plotastic` further lowers the barrier to entry. The author also argues that ChatGPT is a strong argument to switch to CLI, since large language models are highly compatible with text, which is the main format of CLIs. This allows for understanding context, providing code drafts, identifying errors, adding and changing analyses, autocompletion of repetitive commands, follow-up questions and many more.

# 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
- 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
- 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. (n.d.). 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
- 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
- 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
- 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
- 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
- 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
- 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
- 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
- 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
- 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
- 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
- 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/>
- 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
- 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
- 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
- Manifesto for Agile Software Development*. (2001). Retrieved 2024-05-14, from <http://agilemanifesto.org/>
- 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
- 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
- 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., & Zwintz, 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
- 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/>
- 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
- 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>
- 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.
- 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
- 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.
- 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

- 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
- 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
- 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`