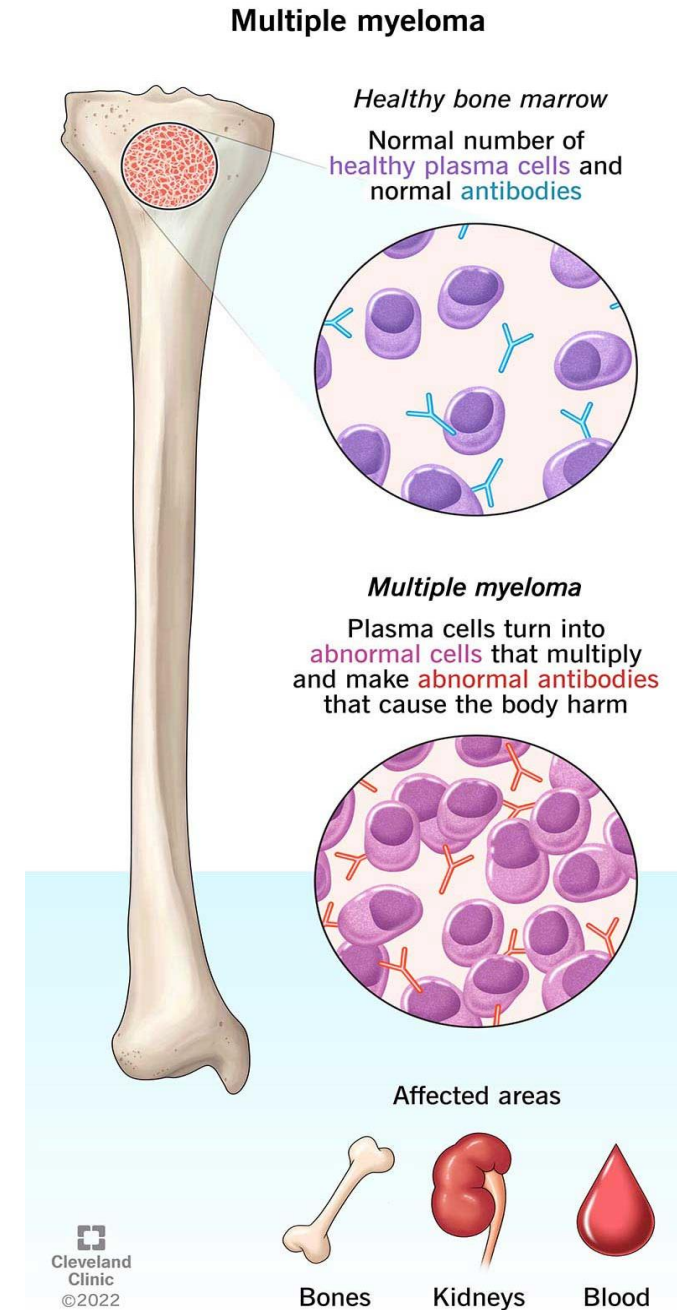


Multiple Myeloma

Elijah Horwath, Mark Massad, Taylor Kielczewski

What is Multiple Myeloma?

- A cancer of plasma cells
- Healthy plasma cells are found in bone marrow and are an important white blood cell that help fight infection
- When plasma cells become cancerous and their growth becomes rapid and unregulated, this is called **multiple myeloma**



Myeloma Cells: Bone Marrow Biopsy

Fig. 1

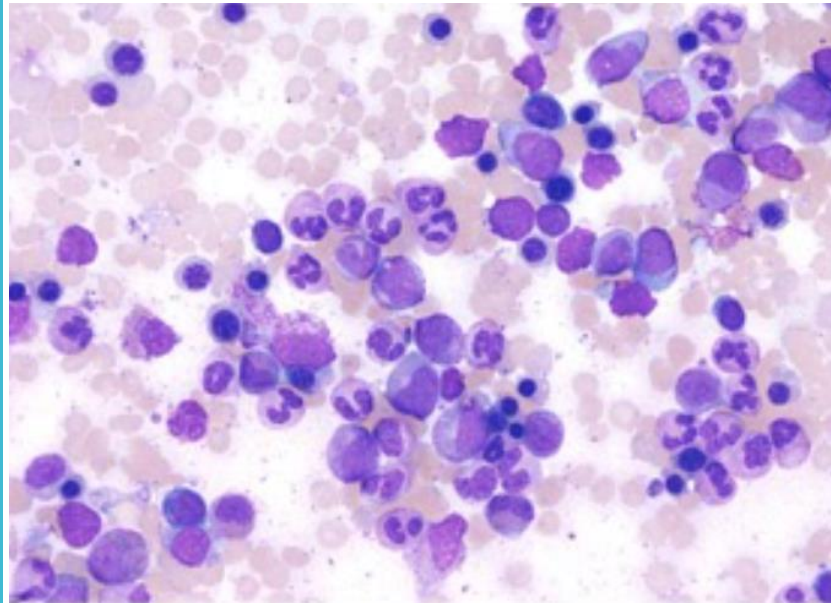
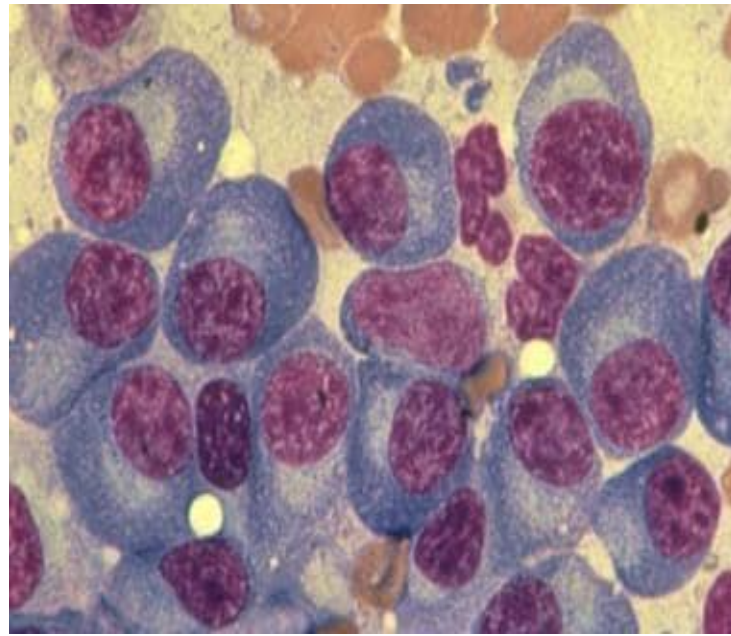


Fig. 2

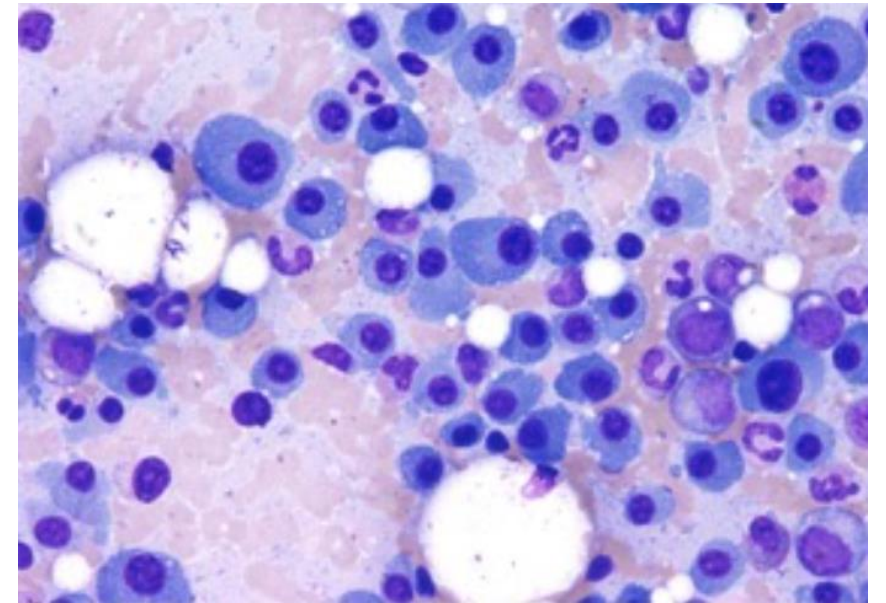


Fig. 3

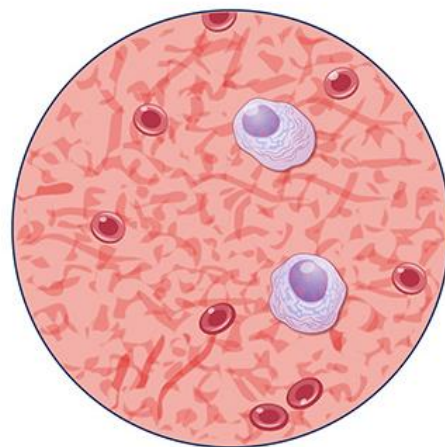
Plasma Cell Conditions

- **MGUS, <10% clonal plasma in bone marrow**
 - 1% chance of progression, can increase per year
- **SMM, typically >10% clonal plasma in bone marrow**
 - 10% chance per year of progression for first 5 years
 - Drops to 3% for next 5 years, and 1% per year after 10 years
- **MM, typically >10% clonal plasma in bone marrow**
 - With “**CRAB**” diagnostics

Blood Smear Illustrations

Monoclonal Gammopathy
of Undetermined Significance

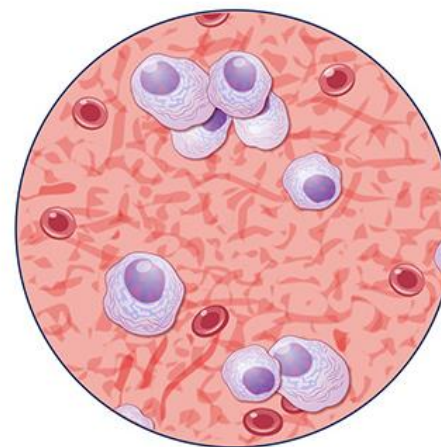
MGUS



No symptoms, and fewer signs
of harmful plasma cells and
proteins in the blood

Smoldering Multiple Myeloma

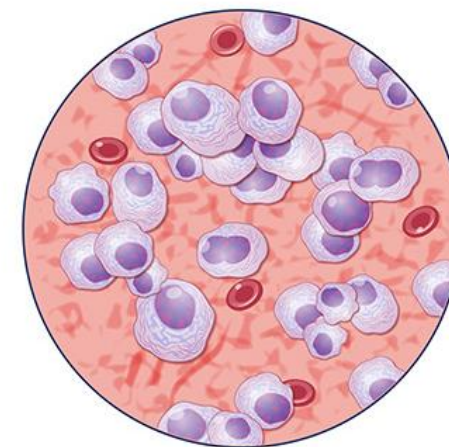
SMM



No symptoms, and more signs
of harmful plasma cells and
proteins in the blood

Multiple Myeloma

MM



Symptoms throughout the body.
Blood is full of cancerous
plasma cells and proteins

Diagnostic Criteria for MM



- **High Calcium**
 - As bones decay, they offput calcium into the bloodstream
 - Causes fatigue, weakness

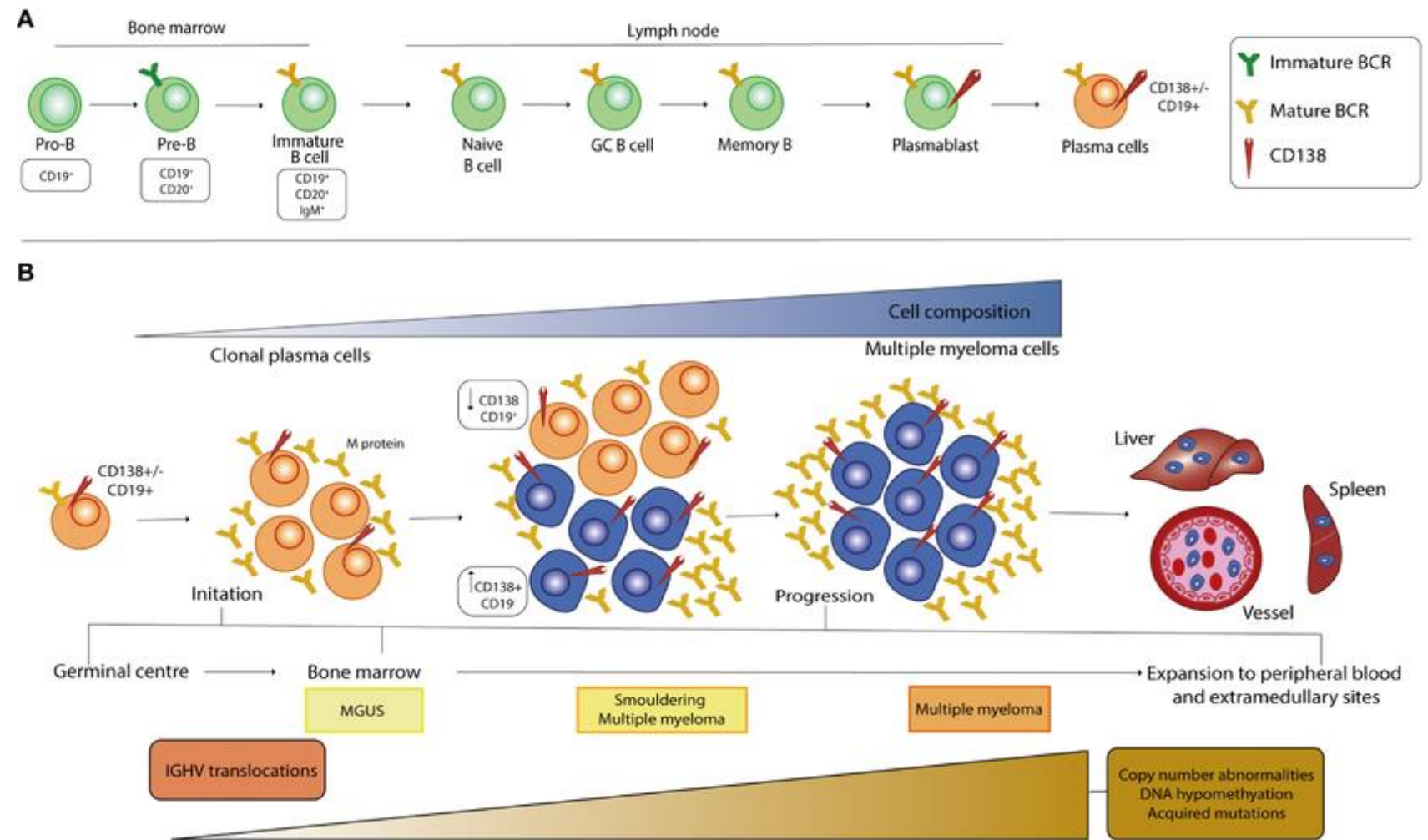
- **Anemia**
 - High plasma counts can impact red and white blood cell and platelet counts
 - Can cause weakness, dizziness, autoimmune deficiency and excessive bleeding (lack of clotting)

- **Renal Dysfunction**
 - High levels of calcium also affect kidneys — the renal system fails to process it all
 - Increased urination, dehydration, abdominal pain and cramping

- **Bone Lesions**
 - Causes bone pain in patient
 - Most common symptom used in diagnosis
 - A bone density exam may mis-identify age-induced osteoporosis as MM

What is CD138?

- Protein that is added to B cells
 - Kind of white blood cell
 - Transforms them into plasma cells
- Involved in cell proliferation, migration, adhesion, and formation of new blood vessel
 - Coreceptor (BCR) binds to growth factors
 - Upregulated in MM cells as well as SMM
- CD138- cells also implicated in other kinds of cancer



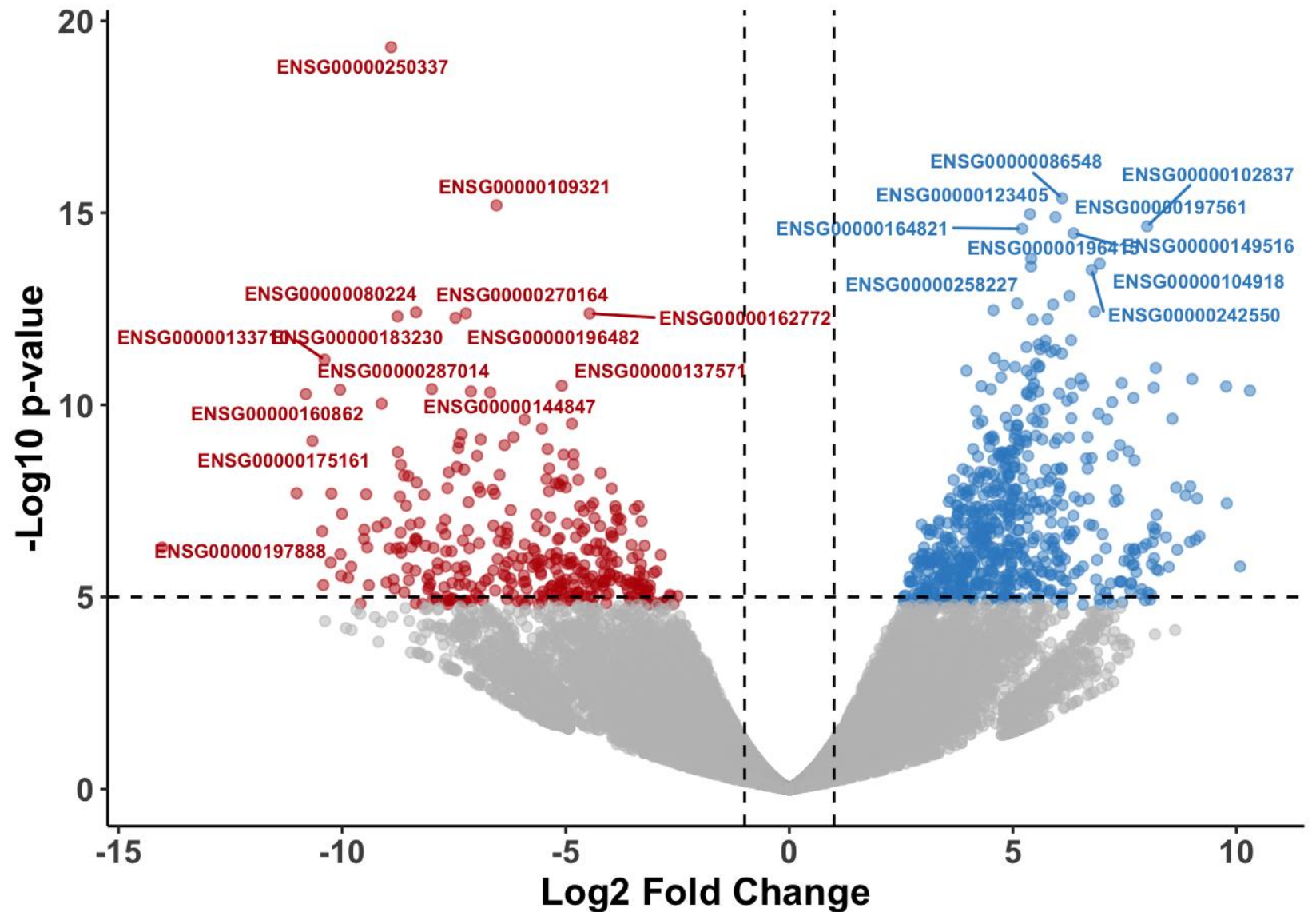
Source: Riccardi et al., *Frontiers in Oncology*, Targeted therapy for multiple myeloma: an overview on CD138-based strategies

Results

Many genes are differentially expressed in patients with MM

Red = upregulated in MM

Blue = downregulated in MM



CD138

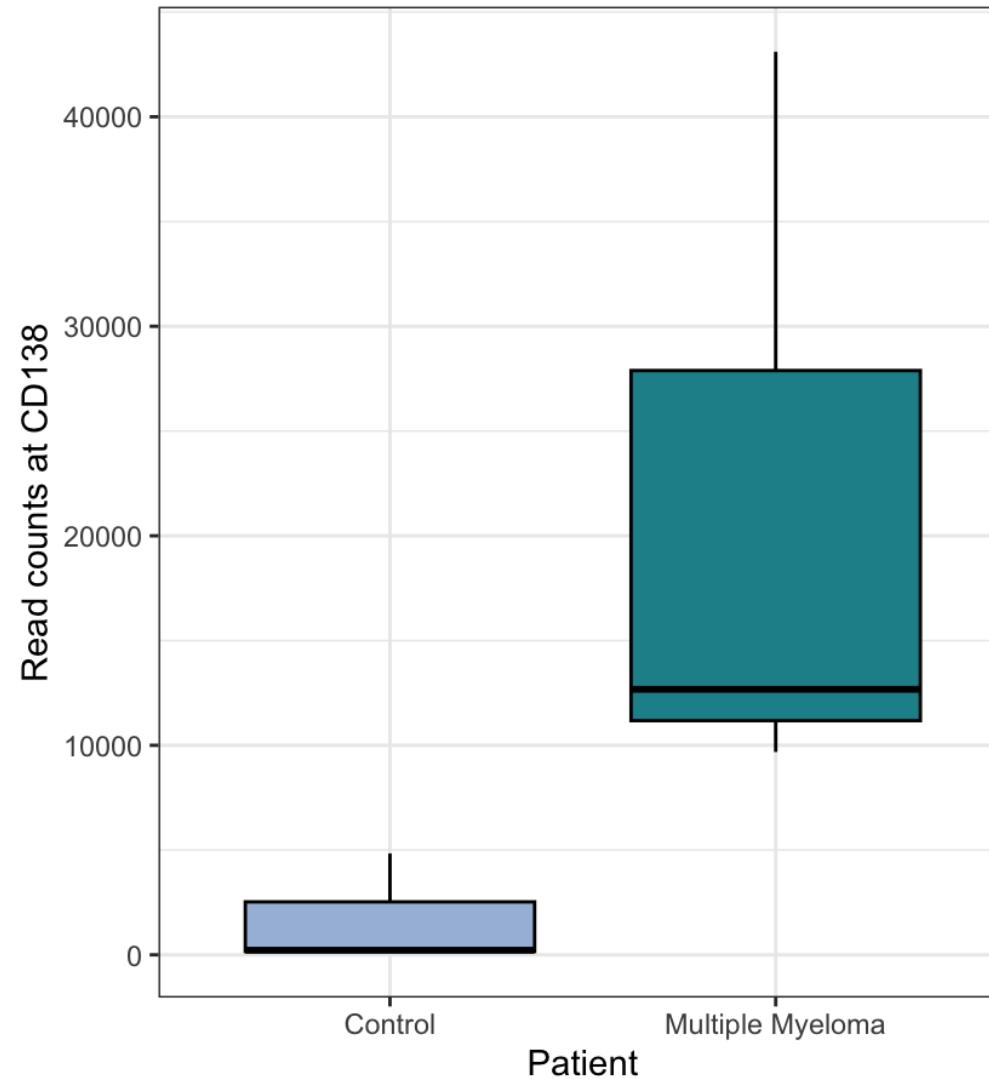
Common
biomarker for MM

Encodes a cell
membrane protein

Responsible for:
Cell Proliferation

Cell Migration

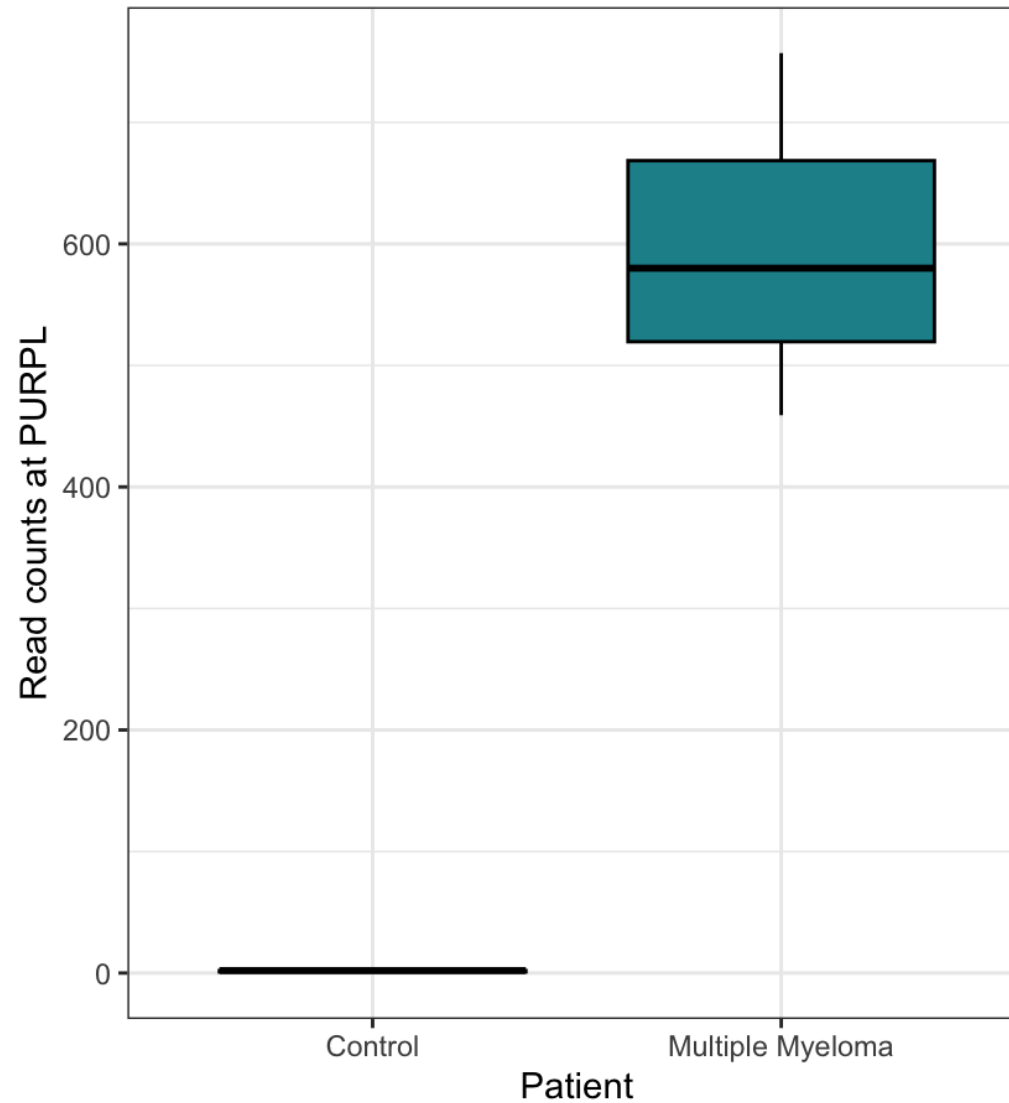
Cell-Matrix
Interactions



P53 regulator

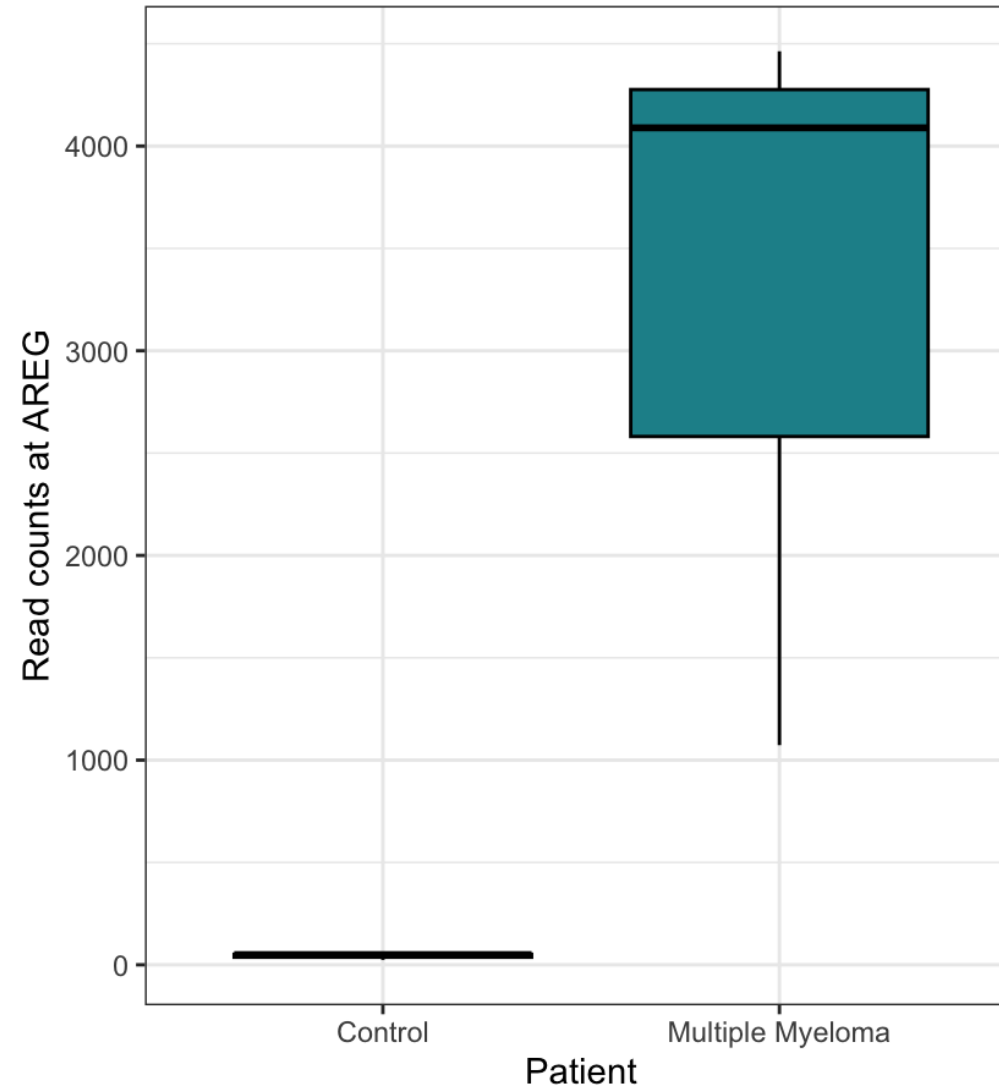
p53 causes apoptosis
in malfunctioning
cells, loss of function
mutations

Mutations of P53 are
common in many
kinds of cancers



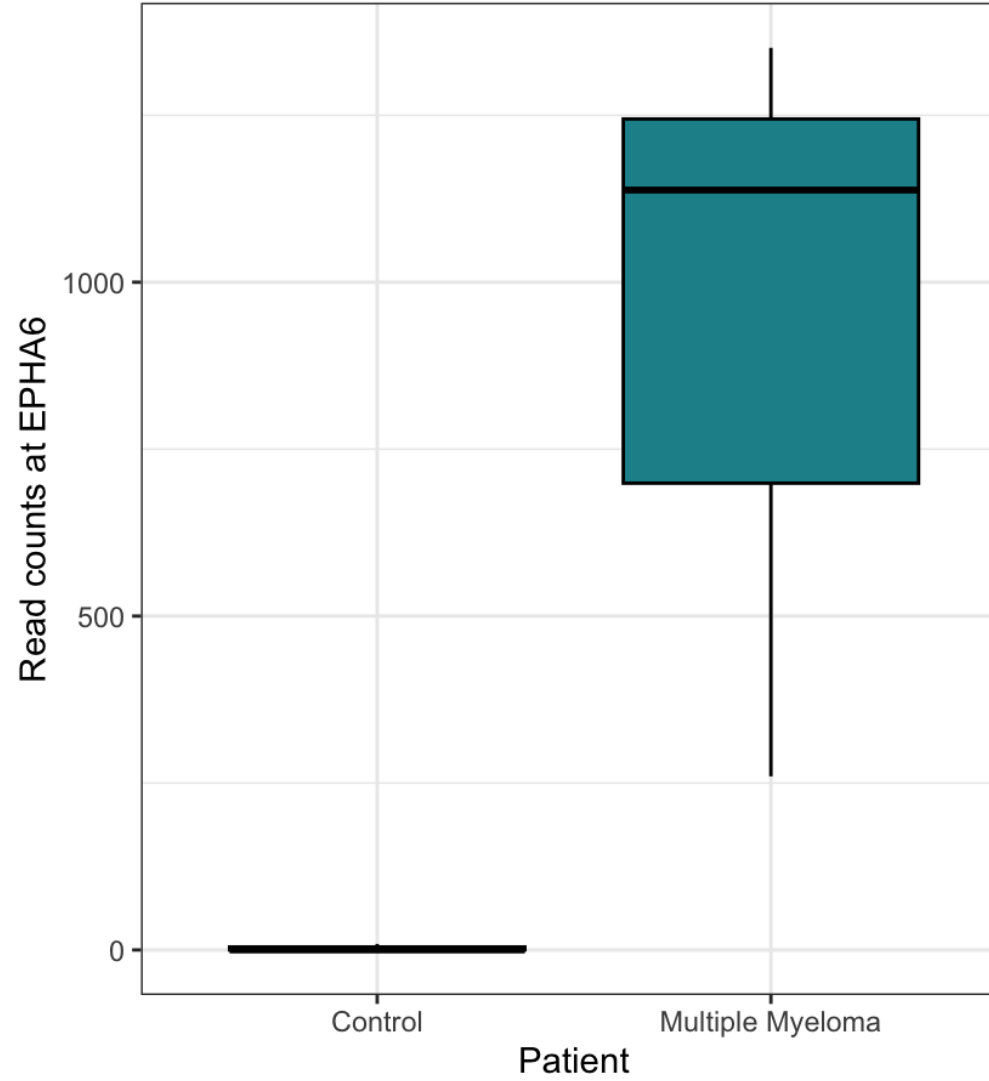
Amphiregulin

growth factor involved in
early system
development and
immune system activity,
commonly upregulated
in cancers



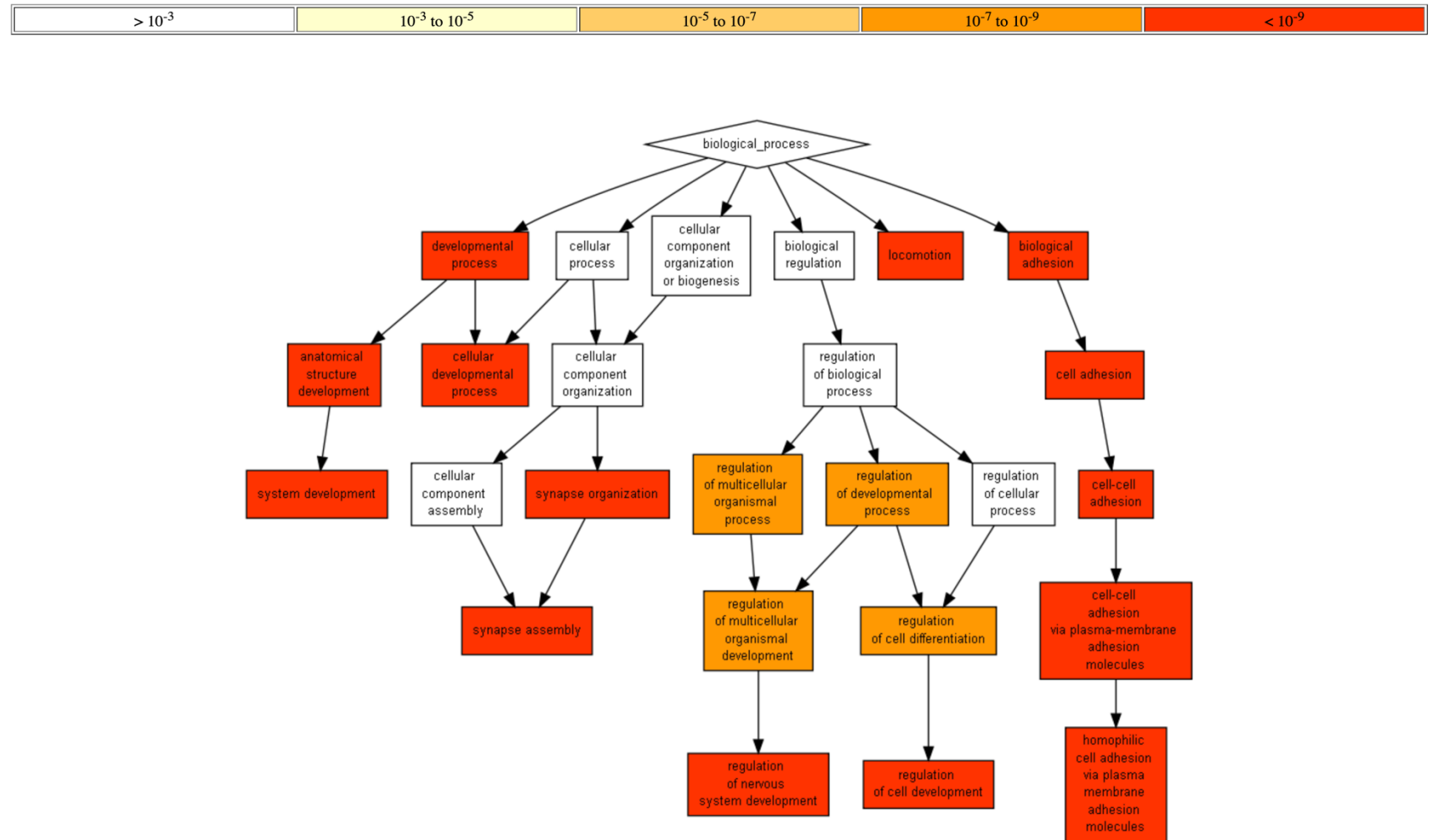
EPH Receptor A6

ephrin receptor,
involved in
angiogenesis and
has been implicated
in cancer



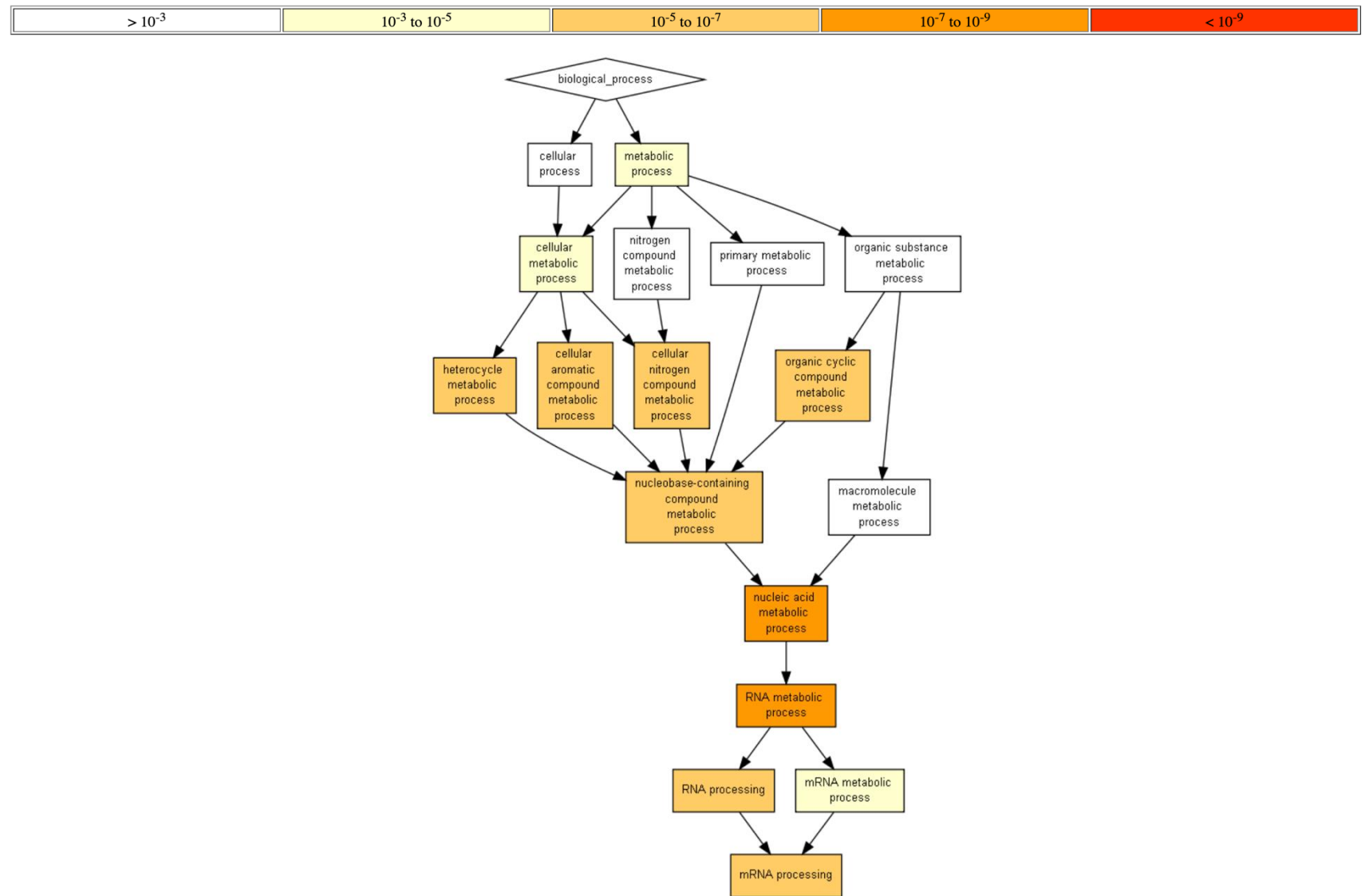
Upregulated Processes

- Cell-cell adhesion
- Nervous system and cell development
- Biological system development
- Synapse organization and assembly
- Locomotion



Downregulated Processes

- Metabolic processes (involved in creation of new molecules)



Source: Eden et al., BMC Bioinformatics, GOrilla: A Tool For Discovery And Visualization of Enriched GO Terms in Ranked Gene Lists

Conclusion

- Multiple Myeloma is a highly aggressive and multifocal cancer, with no known biomarkers
- Many genes responsible for cell development, cell adhesion and locomotion are heavily upregulated, which can cause tumor proliferation & metastasis
- Metabolic processes and immune responses are downregulated, resulting in a loss of cell apoptosis
- There is no current cure, but continued progress in personalized medicine and novel therapies suggests even better outcomes for future patients

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