# 生物医药合作项目开发

**研究方向：** 骨髓瘤思路设计

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# 1 研究背景

Multiple myeloma (MM) 是一种基因复杂、异质性高的疾病，其发展是一个多步骤的过程，涉及肿瘤细胞基因改变的获得和骨髓微环境的变化 (2024, Nature reviews. Disease primers, **IF:76.9**, Q1)[1]。

## 1.1 思路

结合 MM 的 GWAS 研究 (变异与疾病的关系)，预测基因表达变化水平 (即 TWAS，基因与疾病的关系)；MM 的 scRNA-seq 肿瘤细胞分析，并进一步预测肿瘤细胞的代谢变化; 最后，聚焦于基因对肿瘤细胞的代谢改变，以及对应的功能基因。

思路为：TWAS (GWAS + eQTL) + scRNA-seq + metabolic

(TWAS 部分可能会相对耗时，因为该部分的方法为首次接触，需要配置程序)
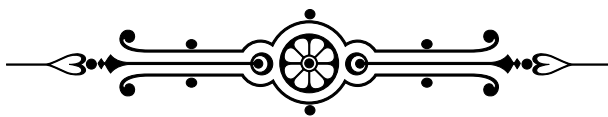
# 2 可行性

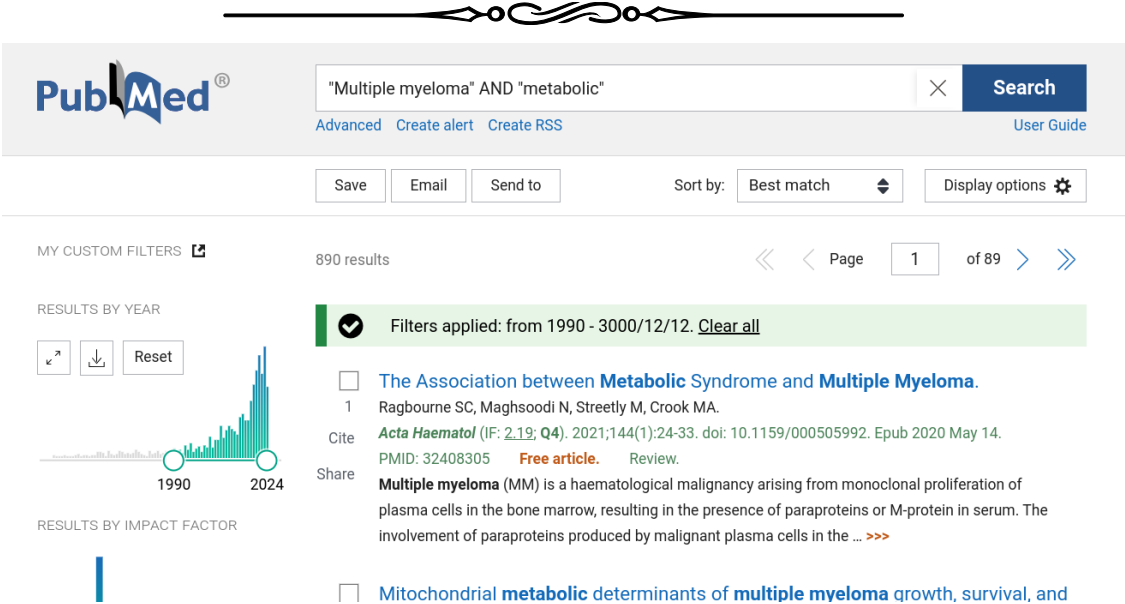## 2.1 以 "Multiple myeloma" AND "metabolic" 搜索文献，发现 MM 与代谢关联密切。



Figure 1: Unnamed chunk 6

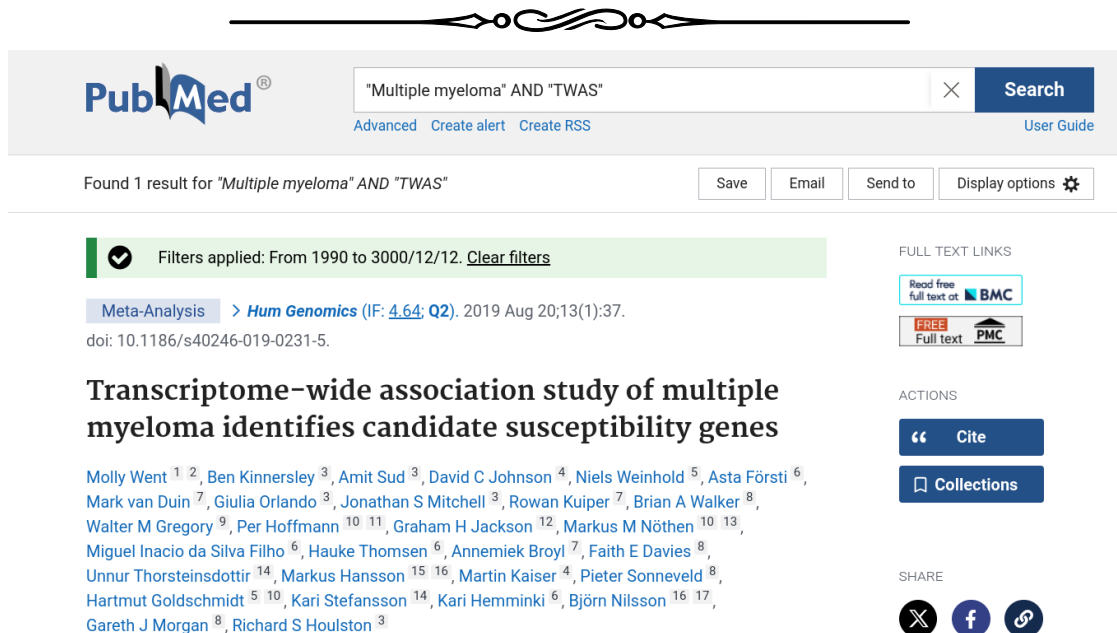## 2.2 以 `"Multiple myeloma" AND "TWAS"` 搜索文献，已有借助 TWAS 研究 MM 的文章。

Pub**Med**®

`"Multiple myeloma" AND "TWAS"`  ✕  **Search**

Advanced  Create alert  Create RSS  User Guide

Found 1 result for *"Multiple myeloma" AND "TWAS"*  Save  Email  Send to  Display options ⚙

✓ Filters applied: From 1990 to 3000/12/12. Clear filters

Meta-Analysis  > *Hum Genomics* (IF: 4.64; **Q2**). 2019 Aug 20;13(1):37.
doi: 10.1186/s40246-019-0231-5.

### Transcriptome-wide association study of multiple myeloma identifies candidate susceptibility genes

Molly Went [1][2], Ben Kinnersley [3], Amit Sud [3], David C Johnson [4], Niels Weinhold [5], Asta Försti [6], Mark van Duin [7], Giulia Orlando [3], Jonathan S Mitchell [3], Rowan Kuiper [7], Brian A Walker [8], Walter M Gregory [9], Per Hoffmann [10][11], Graham H Jackson [12], Markus M Nöthen [10][13], Miguel Inacio da Silva Filho [6], Hauke Thomsen [6], Annemiek Broyl [7], Faith E Davies [8], Unnur Thorsteinsdottir [14], Markus Hansson [15][16], Martin Kaiser [4], Pieter Sonneveld [8], Hartmut Goldschmidt [5][10], Kari Stefansson [14], Kari Hemminki [6], Björn Nilsson [16][17], Gareth J Morgan [8], Richard S Houlston [3]

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Figure 2: Unnamed chunk 7

## 2.3 以 `"Multiple myeloma" AND "metabolic" AND "GWAS"` 搜索文献，发现一篇孟德尔随机化研究，MM 基因与代谢的关系。
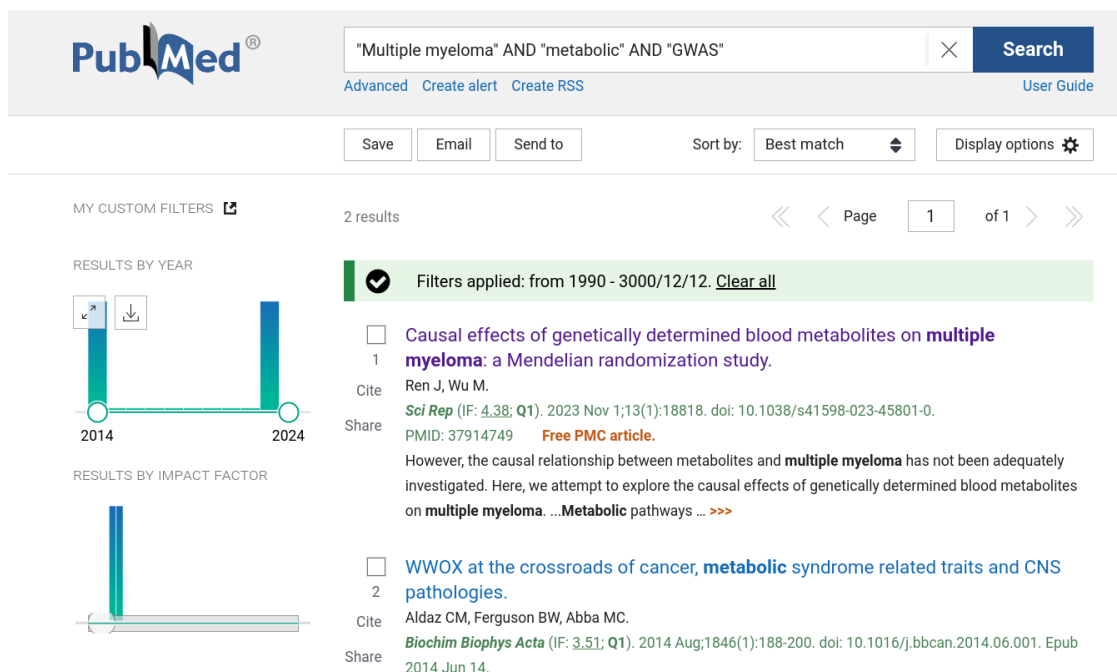
Figure 3: Unnamed chunk 8

# 3 创新性

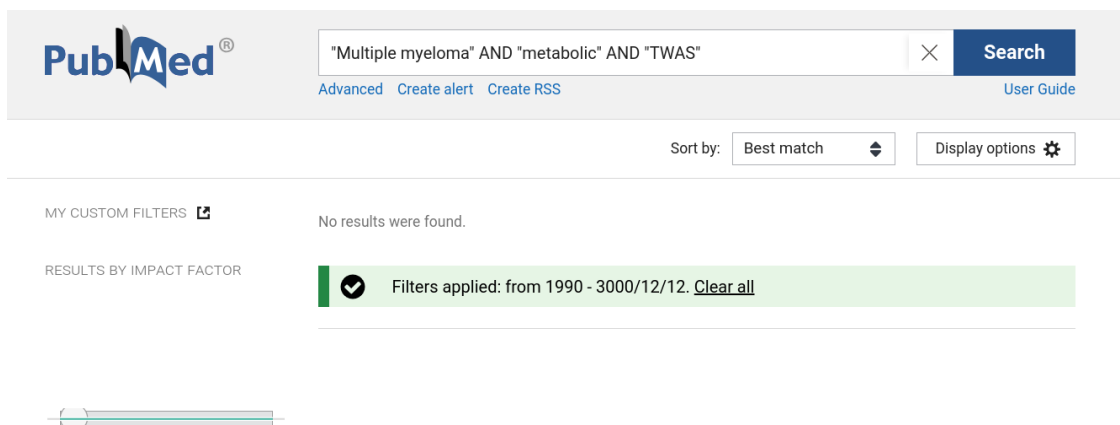## 3.1 以 "Multiple myeloma" AND "metabolic" AND "TWAS" 搜索文献，未发现相关研究。

Figure 4: Unnamed chunk 9

## 3.2 以 "Multiple myeloma" AND "scRNA-seq" AND "metabolic" AND "GWAS" 搜索 PubMed，未发现相关研究。
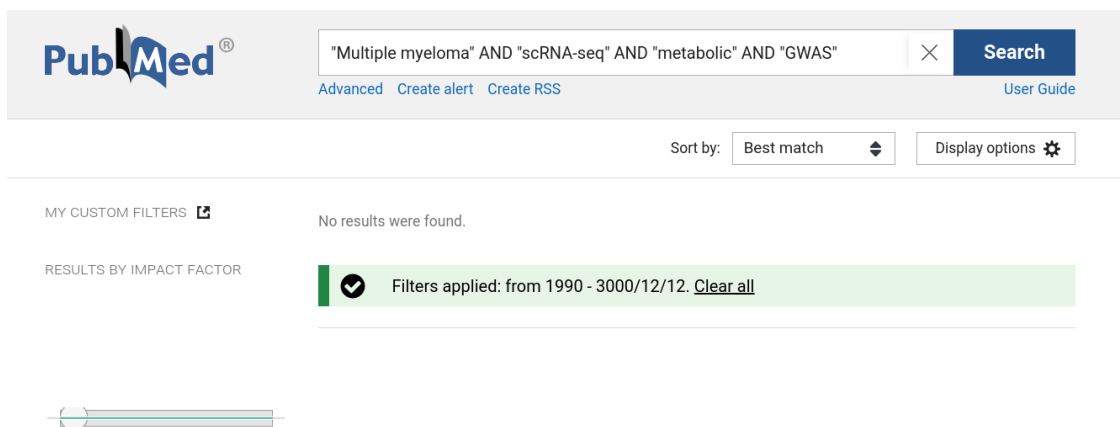


Figure 5: Unnamed chunk 10

# 4 参考文献和数据集

## 4.1 TWAS 方法

- FUSION (2016, Nature Genetics, **IF:31.7**, Q1)[2]
- FOCUS (2020, Human genetics, **IF:3.8**, Q2)[3]

## 4.2 单细胞数据预测代谢通量的方法

- scFEA 通过 scRNA-seq 预测代谢通量 (2021, Genome research, **IF:6.2**, Q1)[4]
- scFEA 的应用实例 (2023, Frontiers in endocrinology, **IF:3.9**, Q2)[5]

## 4.3 GWAS 数据

Table 1: GWAS

| id | trait | ncase | group_... | year | author | consor... | sex | pmid | popula... |
|---|---|---|---|---|---|---|---|---|---|
| ieu-b-... | Multip... | 601 | public | 2021 | Burrows | UK Bio... | Males ... | NA | European |
| finn-b-... | Multip... | 598 | public | 2021 | NA | NA | Males ... | NA | European |
| finn-b-... | Multip... | 598 | public | 2021 | NA | NA | Males ... | NA | European |

## 4.4 scRNA-seq

GEO 上有多数 MM 的 scRNA-seq 数据集，以下举一例。

- GSE271107

**Data Source ID :**

GSE271107


**data_processing :**

Raw scRNA-seq data were preprocessed using the Cell Ranger analysis pipelines (10x Genomics) version 6 with reference genome of human genome (GRCh38) to demultiplex for cell and transcript and generate count table.


**data_processing.1 :**

The count table was loaded into R through Seurat version 4 package for further analysis. Cells that have gene numbers lesser than 200, greater than 7,000, and more than 10mitochondrial genes were discarded from the analysis.


**data_processing.2 :**

For individual sample, a principal component analysis (PCA) was performed on significantly variable genes for remained high-quality cells. Results of individual samples were used for data integration across samples using reciprocal PCA method to minimize technical differences between samples.


**data_processing.3 :**

The integration results were employed as input for clustering using Louvain algorithm with multilevel refinement and the Uniform Manifold Approximation and Projection for Dimension Reduction (UMAP).


**(Others) :**

...


**（上述信息框内容已保存至 Figure+Table/prods-content）**

Table 2: Sample

| rownames | title | disease.state.ch1 | tissue.ch1 |
|---|---|---|---|
| GSM8369863 | Healthy donor_1 | Healthy | Bone marrow aspirate |

| rownames | title | disease.state.ch1 | tissue.ch1 |
| --- | --- | --- | --- |
| GSM8369864 | Healthy donor_2 | Healthy | Bone marrow aspirate |
| GSM8369865 | Healthy donor_3 | Healthy | Bone marrow aspirate |
| GSM8369866 | Healthy donor_4 | Healthy | Bone marrow aspirate |
| GSM8369867 | Healthy donor_5 | Healthy | Bone marrow aspirate |
| GSM8369868 | MGUS_1 | MGUS | Bone marrow aspirate |
| GSM8369869 | MGUS_2 | MGUS | Bone marrow aspirate |
| GSM8369870 | MGUS_3 | MGUS | Bone marrow aspirate |
| GSM8369871 | MGUS_4 | MGUS | Bone marrow aspirate |
| GSM8369872 | MGUS_5 | MGUS | Bone marrow aspirate |
| GSM8369873 | MGUS_6 | MGUS | Bone marrow aspirate |
| GSM8369874 | SMM_1 | SMM | Bone marrow aspirate |
| GSM8369875 | SMM_2 | SMM | Bone marrow aspirate |
| GSM8369876 | SMM_3 | SMM | Bone marrow aspirate |
| GSM8369877 | SMM_4 | SMM | Bone marrow aspirate |
| ... | ... | ... | ... |

# Reference

1. Malard, F. *et al.* Multiple myeloma. *Nature reviews. Disease primers* **10**, (2024).

2. Gusev, A. *et al.* Integrative approaches for large-scale transcriptome-wide association studies. *Nature Genetics* **48**, 245–252 (2016).

3. Wu, C. & Pan, W. A powerful fine-mapping method for transcriptome-wide association studies. *Human genetics* **139**, 199–213 (2020).

4. Alghamdi, N. *et al.* A graph neural network model to estimate cell-wise metabolic flux using single-cell rna-seq data. *Genome research* **31**, 1867–1884 (2021).

5. Agoro, R. *et al.* Single cell cortical bone transcriptomics define novel osteolineage gene sets altered in chronic kidney disease. *Frontiers in endocrinology* **14**, (2023).