

| PMID           | Title                                                                                                                                                                                                        |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PMID: 19941661 | A MIF haplotype is associated with the outcome of patients with severe sepsis: a case control study                                                                                                          |
| PMID: 20388640 | Predictors of response to intra-articular steroid injection in psoriatic arthritis                                                                                                                           |
| PMID: 20447688 | The MIF -173G/C polymorphism and risk of childhood acute lymphoblastic leukemia in a Chinese population                                                                                                      |
| PMID: 16380915 | Replication of putative candidate-gene associations with rheumatoid arthritis in >4,000 samples from North America and Sweden: association of susceptibility with PTPN22, CTLA4, and PADI4                   |
| PMID: 17585860 | Macrophage migration inhibitory factor in acute lung injury: expression, biomarker, and associations.                                                                                                        |
| PMID: 20811626 | Genetic variants in inflammation-related genes are associated with radiation-induced toxicity following treatment for non-small cell lung cancer.                                                            |
| PMID: 23402792 | Macrophage migration inhibitory factor (MIF): genetic evidence for participation in early onset and early stage rheumatoid arthritis                                                                         |
| PMID: 24151396 | Macrophage migration inhibitory factor gene polymorphisms in inflammatory bowel disease: An association study in New Zealand Caucasians and meta-analysis                                                    |
| PMID: 26107210 | Contribution of Macrophage Migration Inhibitory Factor -173G/C Gene Polymorphism to the Risk of Cancer in Chinese Population                                                                                 |
| PMID: 26542751 | Functional polymorphisms in the gene encoding macrophage migration inhibitory factor (MIF) are associated with active pulmonary tuberculosis                                                                 |
| PMID: 29545822 | Macrophage Migration Inhibitory Factor -173 G/C Polymorphism: A Global Meta-Analysis across the Disease Spectrum.                                                                                            |
| PMID: 32560699 | MIF -173G/C (rs755622) polymorphism modulates coronary artery disease risk: evidence from a systematic meta-analysis.                                                                                        |
| PMID: 22113576 | Polymorphisms in immune function genes and non-Hodgkin lymphoma survival.                                                                                                                                    |
| PMID: 24530749 | Macrophage migration inhibitory factor: association of -794 CATT5-8 and -173 G>C polymorphisms with TNF-α in systemic lupus erythematosus                                                                    |
| PMID: 27696094 | A Macrophage Migration Inhibitory Factor Polymorphism Is Associated with Autoimmune Hepatitis Severity in US and Japanese Patients                                                                           |
| PMID: 29661540 | MIF functional polymorphisms (-794 CATT 5-8 and -173 G>C) are associated with MIF serum levels, severity and progression in male multiple sclerosis from western Mexican population                          |
| PMID: 29996006 | MIF-173G/C (rs755622) polymorphism as a risk factor for acute lymphoblastic leukemia development in children                                                                                                 |
| PMID: 30747392 | Macrophage migration inhibitory factor polymorphisms are a potential susceptibility marker in systemic sclerosis from southern Mexican population: association with MIF mRNA expression and cytokine profile |
| PMID: 31978276 | Association of the genetic variants (-794 CATT5-8 and -173 G > C) of macrophage migration inhibitory factor (MIF) with higher soluble levels of MIF and TNFα in women with breast cancer                     |

**Supplemental Table 1. *MIF* SNP rs755622 highlighted literature in inflammatory-associated conditions.** Summary highlighting selected articles pertaining to rs755622 history and research in inflammatory conditions to provide the relative clinical importance of this germline SNP.

Supplemental Table 2- Clinical Cohort summary for samples used in RNA-sequencing study

| Characteristic                   | CC, N = 1 <sup>I</sup> | CG, N = 16 <sup>I</sup> | GG, N = 17 <sup>I</sup> |
|----------------------------------|------------------------|-------------------------|-------------------------|
| race                             |                        |                         |                         |
| black                            | 0 (0%)                 | 1 (6.2%)                | 1 (5.9%)                |
| non hispanic white               | 1 (100%)               | 15 (94%)                | 16 (94%)                |
| age                              | 59 (59, 59)            | 64 (53, 69)             | 59 (49, 66)             |
| sex                              | 1 (100%)               | 6 (38%)                 | 6 (35%)                 |
| kps.at.diagnosis                 |                        |                         |                         |
| 60                               | 0 (0%)                 | 1 (6.2%)                | 0 (0%)                  |
| 70                               | 0 (0%)                 | 1 (6.2%)                | 1 (5.9%)                |
| 80                               | 0 (0%)                 | 8 (50%)                 | 4 (24%)                 |
| 90                               | 1 (100%)               | 6 (38%)                 | 12 (71%)                |
| deletion_1p                      | 0 (0%)                 | 1 (6.2%)                | 2 (12%)                 |
| deletion_19q                     | 0 (0%)                 | 5 (31%)                 | 1 (6.2%)                |
| idh1_mutated                     | 0 (0%)                 | 0 (0%)                  | 1 (5.9%)                |
| mgmt_methylated                  | 0 (NA%)                | 2 (33%)                 | 4 (80%)                 |
| ki_67                            | 5 (5, 5)               | 25 (19, 32)             | 25 (14, 32)             |
| egfr_amplified                   | 0 (0%)                 | 9 (56%)                 | 5 (31%)                 |
| pfs                              | 19 (19, 19)            | 8 (5, 21)               | 25 (5, 51)              |
| os                               | 27 (27, 27)            | 12 (10, 25)             | 36 (9, 82)              |
| <sup>I</sup> n (%); Median (IQR) |                        |                         |                         |

**Supplemental Table 2. Clinical cohort summary for samples used for RNA-sequencing.** Summary of the patients used for RNAseq analysis from the CCF cohort (n=17 G/\* and n=17 G/G patients). Molecular markers and clinical data available were selected along with overall survival and sex to evenly distribute similar cohorts of patients and minimize confounder.

A

Table 1: Patient Characteristics by dataset

|                                                      | Level         | Overall<br>N = 966      | Case<br>N = 131         | Cleveland Clinic<br>N = 449 | Moffitt<br>N = 386      | P                   |
|------------------------------------------------------|---------------|-------------------------|-------------------------|-----------------------------|-------------------------|---------------------|
| Age at diagnosis                                     |               |                         |                         |                             |                         |                     |
|                                                      | mean (SD)     | 60.45 (12.87)           | 62.00 (11.13)           | 60.78 (13.30)               | 59.54 (12.88)           | 0.129 <sup>a</sup>  |
|                                                      | median [IQR]  | 61.07 [53.00,<br>69.00] | 64.00 [55.00,<br>69.00] | 61.41 [53.29,<br>70.22]     | 61.00 [52.00,<br>69.00] | 0.239 <sup>b</sup>  |
| Sex (%)                                              | Female        | 344 (35.6)              | 47 (35.9)               | 150 (33.4)                  | 147 (38.1)              | 0.371 <sup>c</sup>  |
|                                                      | Male          | 622 (64.4)              | 84 (64.1)               | 299 (66.6)                  | 239 (61.9)              |                     |
| Surgery status (%)                                   | Gross total   | 358 (37.1)              | 75 (57.3)               | 156 (34.7)                  | 127 (32.9)              | <0.001 <sup>c</sup> |
|                                                      | Subtotal      | 328 (34.0)              | 53 (40.5)               | 163 (36.3)                  | 112 (29.0)              |                     |
|                                                      | Other         | 280 (29.0)              | 3 (2.3)                 | 130 (29.0)                  | 147 (38.1)              |                     |
| Standard of care (%) <sup>a</sup>                    | Yes           | 816 (84.5)              | 78 (59.5)               | 384 (85.5)                  | 354 (91.7)              | <0.001 <sup>c</sup> |
|                                                      | No            | 142 (14.7)              | 45 (34.4)               | 65 (14.5)                   | 32 (8.3)                |                     |
|                                                      | unknown       | 8 (0.8)                 | 8 (6.1)                 | 0 (0.0)                     | 0 (0.0)                 |                     |
| KPS (%)                                              | <=70          | 206 (21.3)              | 56 (42.7)               | 65 (14.5)                   | 85 (22.0)               | <0.001 <sup>c</sup> |
|                                                      | 70 - 80       | 265 (27.4)              | 16 (12.2)               | 142 (31.6)                  | 107 (27.7)              |                     |
|                                                      | 80 - 90       | 389 (40.3)              | 21 (16.0)               | 228 (50.8)                  | 140 (36.3)              |                     |
|                                                      | 90 - 100      | 38 (3.9)                | 1 (0.8)                 | 7 (1.6)                     | 30 (7.8)                |                     |
|                                                      | Not Available | 68 (7.0)                | 37 (28.2)               | 7 (1.6)                     | 24 (6.2)                |                     |
|                                                      |               |                         |                         |                             |                         |                     |
| SNP Status                                           | CC or CG      | 324 (33.5)              | 42 (32.1)               | 146 (32.5)                  | 136 (35.2)              | 0.658 <sup>b</sup>  |
|                                                      | GG            | 642 (66.5)              | 89 (67.9)               | 303 (67.5)                  | 250 (64.8)              |                     |
| Overall Survival in months<br>(median [IQR])         |               | 13.84 [7.38,<br>23.20]  | 12.40 [5.49,<br>20.75]  | 13.77 [7.00,<br>26.13]      | 14.54 [8.95,<br>21.96]  | 0.024 <sup>b</sup>  |
| Vital Status (%)                                     |               |                         |                         |                             |                         | 0.016 <sup>c</sup>  |
|                                                      | Alive         | 75 (7.8)                | 3 (2.3)                 | 44 (9.8)                    | 28 (7.3)                |                     |
|                                                      | Deceased      | 891 (92.2)              | 128 (97.7)              | 405 (90.2)                  | 358 (92.7)              |                     |
| Recurrence free Survival in<br>months (median [IQR]) |               | 6.87 [3.32,<br>12.45]   | 6.16 [3.95,<br>12.42]   | 5.57 [2.83,<br>12.23]       | 8.20 [5.23,<br>13.03]   | <0.001 <sup>b</sup> |
| Recurrence Status                                    | Yes           | 629 (65.1)              | 74 (56.5)               | 330 (73.5)                  | 225 (58.3)              | <0.001 <sup>c</sup> |
|                                                      | No            | 173 (17.9)              | 56 (42.7)               | 117 (26.1)                  | 0 (0.0)                 |                     |
|                                                      | Unknown       | 164 (17.0)              | 1 (0.8)                 | 2 (0.4)                     | 161 (41.7)              |                     |

a.One-way analysis of Variance.  
b.Kruskal-Wallis Test  
c.Chi-square or Fisher's exact test as appropriate.  
<sup>a</sup>Standard of Care includes surgery with a full 6 weeks of Radiation and Temodar.  
31 patients with missing information (7 – SNP status, 23 – Overall survival, 2 – vital status) were excluded from the analysis.

B

Table 2: Patient Characteristics by genotype (all data combined)

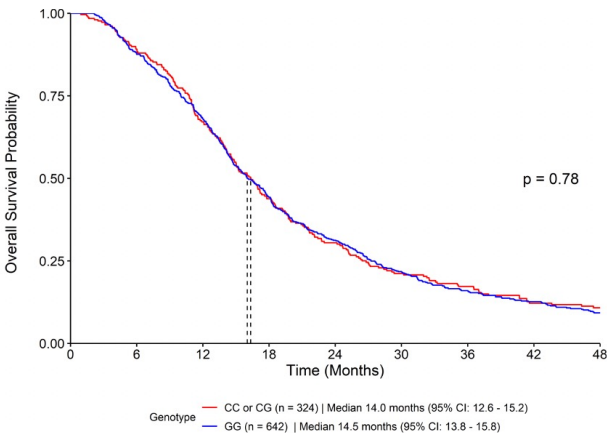
|                                                      | Level         | Overall<br>N = 966      | CC or CG<br>N = 324     | GG<br>N = 642           | P-value            |
|------------------------------------------------------|---------------|-------------------------|-------------------------|-------------------------|--------------------|
| Age at diagnosis                                     |               |                         |                         |                         |                    |
|                                                      | mean (SD)     | 60.45 (12.87)           | 60.93 (12.48)           | 60.21 (13.07)           | 0.406 <sup>a</sup> |
|                                                      | median [IQR]  | 61.07 [53.00,<br>69.00] | 62.00 [53.00,<br>69.53] | 61.00 [53.00,<br>69.00] | 0.441 <sup>b</sup> |
| Sex (%)                                              | Female        | 344 (35.6)              | 135 (41.7)              | 209 (32.6)              | 0.007 <sup>c</sup> |
|                                                      | Male          | 622 (64.4)              | 189 (58.3)              | 433 (67.4)              |                    |
| Surgery status (%)                                   | Gross total   | 358 (37.1)              | 115 (35.5)              | 243 (37.9)              | 0.514 <sup>c</sup> |
|                                                      | Subtotal      | 328 (34.0)              | 118 (36.4)              | 210 (32.7)              |                    |
|                                                      | Other         | 280 (29.0)              | 91 (28.1)               | 189 (29.4)              |                    |
| Standard of care (%) <sup>a</sup>                    | Yes           | 816 (84.5)              | 258 (79.6)              | 558 (86.9)              | 0.012 <sup>c</sup> |
|                                                      | No            | 142 (14.7)              | 63 (19.4)               | 79 (12.3)               |                    |
|                                                      | unknown       | 8 (0.8)                 | 3 (0.9)                 | 5 (0.8)                 |                    |
| KPS (%)                                              | <=70          | 206 (21.3)              | 65 (20.1)               | 141 (22.0)              | 0.900 <sup>c</sup> |
|                                                      | 70 - 80       | 265 (27.4)              | 89 (27.5)               | 176 (27.4)              |                    |
|                                                      | 80 - 90       | 389 (40.3)              | 131 (40.4)              | 258 (40.2)              |                    |
|                                                      | 90 - 100      | 38 (3.9)                | 15 (4.6)                | 23 (3.6)                |                    |
|                                                      | Not Available | 68 (7.0)                | 24 (7.4)                | 44 (6.9)                |                    |
|                                                      |               |                         |                         |                         |                    |
| Overall Survival in months<br>(median [IQR])         |               | 13.84 [7.38,<br>23.20]  | 13.26 [7.07,<br>21.73]  | 14.13 [7.62,<br>24.24]  | 0.345 <sup>b</sup> |
| Vital Status (%)                                     |               |                         |                         |                         | 0.93 <sup>c</sup>  |
|                                                      | Alive         | 75 (7.8)                | 26 (8.0)                | 49 (7.6)                |                    |
|                                                      | Deceased      | 891 (92.2)              | 298 (92.0)              | 593 (92.4)              |                    |
| Recurrence free Survival in<br>months (median [IQR]) |               | 6.87 [3.32,<br>12.45]   | 6.77 [3.41, 11.13]      | 7.00 [3.30,<br>13.04]   | 0.247 <sup>b</sup> |
| Recurrence Status                                    | Yes           | 629 (65.1)              | 200 (61.7)              | 429 (66.8)              | 0.253 <sup>c</sup> |
|                                                      | No            | 173 (17.9)              | 66 (20.4)               | 107 (16.7)              |                    |
|                                                      | Unknown       | 164 (17.0)              | 58 (17.9)               | 106 (16.5)              |                    |

a.Independent t test.  
b.Mann-Whitney U test  
c.Chi-square or Fisher's exact test as appropriate.  
<sup>a</sup>Standard of Care includes surgery with a full 6 weeks of Radiation and Temodar.  
31 patients with missing information (7 – SNP status, 23 – Overall survival, 2 – vital status) were excluded from the analysis.

C

| Single Nucleotide Polymorphism | Allele Frequency Controls (%)<br>1000 Genomes European,<br>n=1,006 | Allele Frequency GBM patients(%)<br>CCF, n=449 | Allele Frequency GBM patients (%)<br>Moffitt, n=386 | Allele frequency GBM patients (%) Case Western, n=131 |
|--------------------------------|--------------------------------------------------------------------|------------------------------------------------|-----------------------------------------------------|-------------------------------------------------------|
| Major Allele (G)               | 81.9                                                               | 82.6                                           | 80.9                                                | 82.4                                                  |
| Minor Allele (C)               | 18.6                                                               | 17.4                                           | 19.0                                                | 17.6                                                  |

D



E

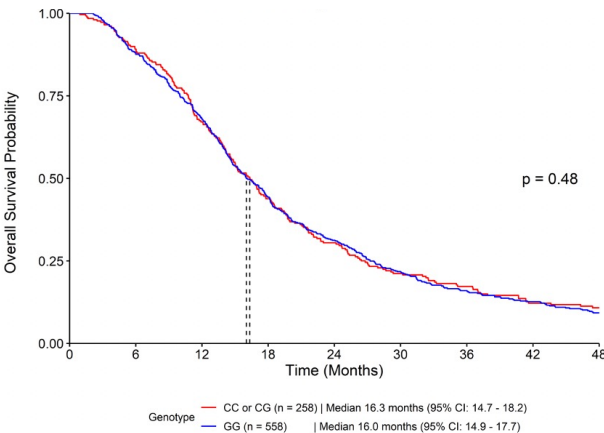


Table 3: Univariate and multivariable Cox proportional hazards models predicting overall and progression-free survival for MIF SNP rs755622 in GBM cohorts

| Genotype | Overall Survival      |       |                       |       | Progression-Free Survival |       |                       |       |
|----------|-----------------------|-------|-----------------------|-------|---------------------------|-------|-----------------------|-------|
|          | Univariate            |       | Multivariable*        |       | Univariate                |       | Multivariable*        |       |
|          | Hazard Ratio (95% CI) | P     | Hazard Ratio (95% CI) | P     | Hazard Ratio (95% CI)     | P     | Hazard Ratio (95% CI) | P     |
| GG       | ref                   | --    | ref                   | --    | ref                       | --    | ref                   | --    |
| CC or CG | 1.02 (0.89-1.17)      | 0.781 | 1.07 (0.81-1.08)      | 0.373 | 1.02 (0.86-1.21)          | 0.787 | 1.06 (0.90-1.26)      | 0.485 |

\*Adjusted for age, sex, surgery, and standard of care

**Supplemental Figure 1. Univariate and multivariable analysis of the *MIF* SNP rs755622 in GBM cohorts.** Germline DNA was acquired from PBMCs or saliva samples from n=449 (Cleveland Clinic), n=386 (Moffitt Cancer Center), and n=131 (Case Western) GBM patients and then tested for the *MIF* SNP rs755622 using PCR with restriction enzyme digestion as described in detail in the methods. **(A)** Descriptive statistics of clinical features of GBM including sex, surgery type, standard of care, KPS, and SNP status including all cohorts of GBM patients. Primary features known to associate with outcome such as higher KPS, total as compared to subtotal tumor resection and treatment with standard of care all confer a survival advantage. **(B)** Descriptive statistics combining data from all three cohorts of GBM patients demonstrated statistically significant differences in allele frequencies of the *MIF* SNP rs755622 (minor 'C' allele containing genotypes vs the homozygous major 'G' allele genotype) for standard-of-care treatment and sex status. **(C)** The allele frequencies for *MIF* rs755622 are similar in the three GBM cohorts and the 1000 Genomes European cohort using Hardy-Weinberg principle and chi-square test for differences from the reference control cohort. **(D)** Univariate analysis of overall survival across all cohorts shows no survival difference by log-rank test. **(E)**. Restricting to patients uniformly treated with standard of care, we observed no significant difference in overall survival according to *MIF* rs755622 genotype (CC/CG versus GG) by the log-rank test. **(F)**. Univariate and multivariable Cox proportional hazards models predicting overall and progression-free survival for *MIF* SNP rs755622 in GBM cohorts.

Supplemental Figure 2- MIF CATT repeat analysis in GBM patients shows correlation with rs755622

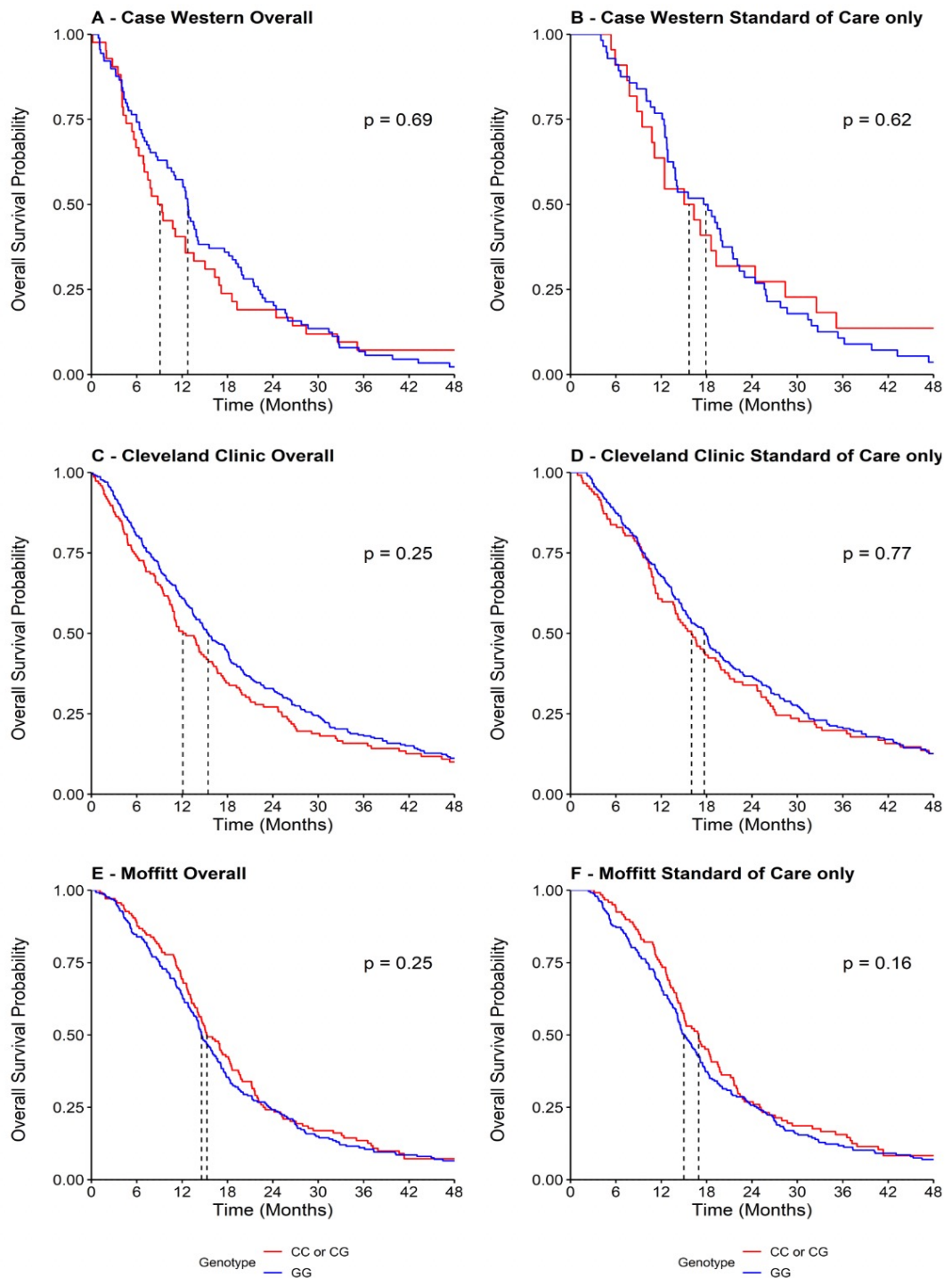
A

| Genotype     | Patient # | Percent GBM Patients | Percent Controls |
|--------------|-----------|----------------------|------------------|
| 5/5          | 37        | 7.1                  | 8.2              |
| 5/6          | 147       | 28.4                 | 29.0             |
| 5/7          | 31        | 6.0                  | 8.9              |
| 5/8          | 1         | 0.1                  | 0.0              |
| 6/6          | 212       | 40.9                 | 36.6             |
| 6/7          | 78        | 15.6                 | 15.7             |
| 6/8          | 2         | 0.1                  | 0.0              |
| 7/7          | 10        | 1.9                  | 0.5              |
| 7/8          | 0         | 0.0                  | 1.1              |
| 5 containing | 184       | 35.5                 | 37.2             |
| 7 containing | 23        | 23.6                 | 26.2             |

B

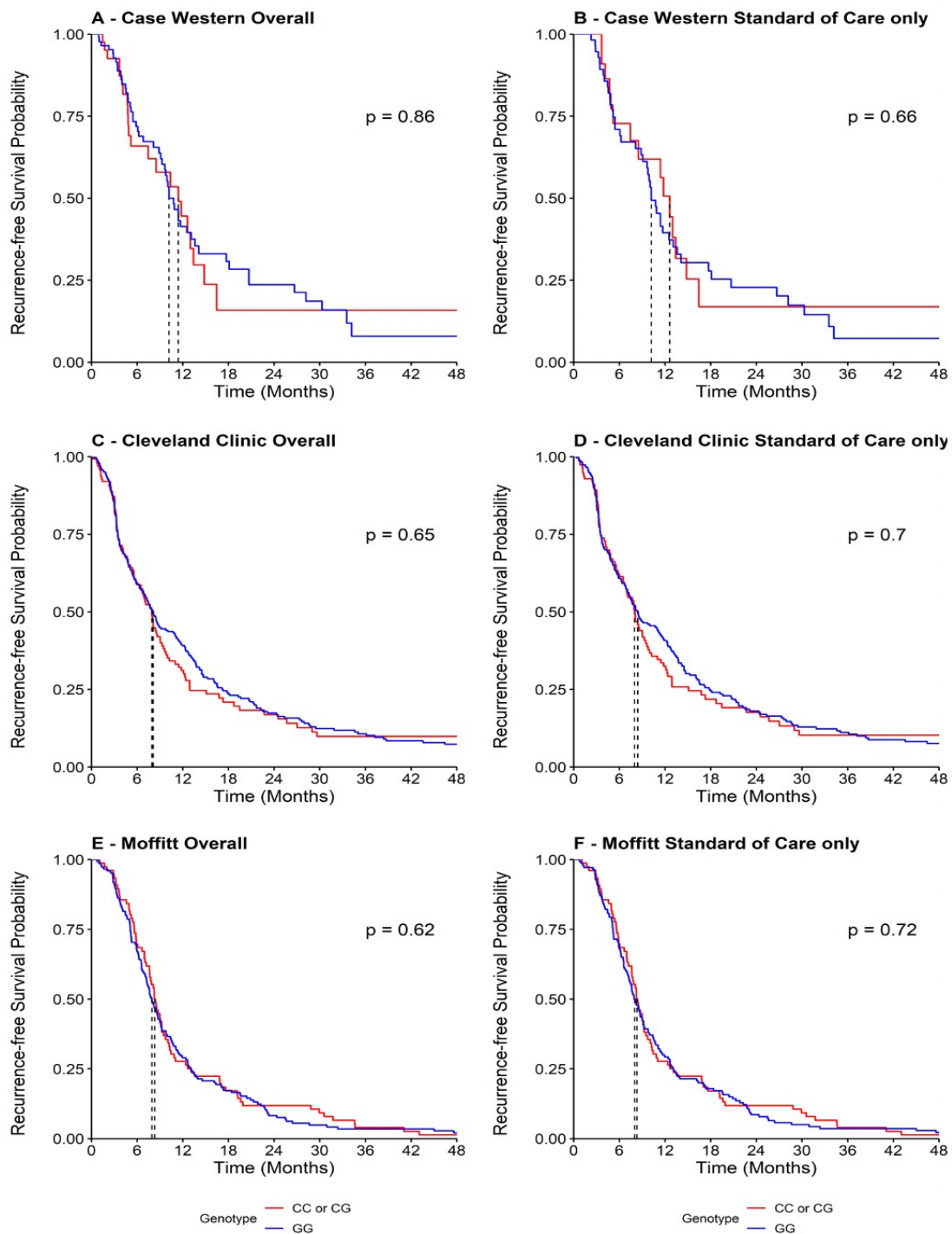
| Segregation Status                                  | Number of Patient Alleles | Percent |
|-----------------------------------------------------|---------------------------|---------|
| Co-segregation of G SNP with 5/6 CATT repeats       | 844                       | 94.2    |
| Separate segregation of G SNP with 5/6 CATT repeats | 52                        | 5.8     |
| Co-segregation of C SNP with 7/8 CATT repeats       | 127                       | 96.2    |
| Separate segregation of C SNP with 7/8 CATT repeats | 5                         | 3.8     |

**Supplemental Figure 2. MIF CATT repeat analysis in GBM patients shows correlation with rs755622.** (A) The CATT microsatellite in the *MIF* promoter upstream of the *MIF* SNP rs755622 was analyzed by capillary electrophoresis in the Cleveland Clinic cohort. (B) Those patients with both rs755622 SNP information and CATT repeat information were correlated to confirm linkage disequilibrium, which showed approximately 95% segregation of the 5/6 repeat and the major allele at rs755622, while 7/8 CATT repeats were linked with the minor allele of rs755622.



\*Vertical lines indicate median survival time

**Supplemental Figure 3. Univariate analysis of clinical cohorts for *MIF* SNP rs755622 (overall survival).** (A-F) Univariate analysis of overall survival comparing patients with the minor allele to patients homozygous for the major allele across all samples (left column) and then those who received full standard-of-care treatment protocol (right column), with log rank p-value comparing each group provided to the right of each curve.



**Supplemental Figure 4. Univariate analysis of clinical cohorts for *MIF* SNP rs755622 (progression-free survival).** (A-F) Univariate analysis of recurrence-free survival comparing patients with the minor allele to patients homozygous for the major allele across all samples (left column) and then those who received full standard-of-care treatment protocol (right column), with log rank p value comparing each group provided to the right of each curve.

A

IPA Analysis top 100 Genes (C/G)

| Diseases or Functions Annotation                 | p-value     |
|--------------------------------------------------|-------------|
| Synthesis of prostaglandin E2                    | 5.96E-10    |
| Synthesis of eicosanoid                          | 7.53E-10    |
| Innate immune response                           | 7.83E-10    |
| Systemic autoimmune syndrome                     | 1.42E-09    |
| Apoptosis of neutrophils                         | 9.96E-09    |
| Stimulation of myeloid cells                     | 1.09E-08    |
| Activation of cells                              | 1.87E-08    |
| Activation of macrophages                        | 2.08E-08    |
| Inflammation of gastrointestinal tract           | 2.79E-08    |
| Inhibition of cells                              | 3.72E-08    |
| Stimulation of acute myeloblastic leukemia cells | 4.52E-08    |
| Chronic inflammatory disorder                    | 5.42E-08    |
| Activation of antigen presenting cells           | 5.93E-08    |
| Rheumatoid arthritis                             | 0.00000006  |
| Rheumatic Disease                                | 6.38E-08    |
| Activation of neutrophils                        | 0.000000098 |
| Stimulation of granulocytes                      | 0.000000101 |
| Stimulation of cancer cells                      | 0.00000011  |
| Delay in apoptosis of neutrophils                | 0.00000011  |
| Stimulation of phagocytes                        | 0.000000127 |
| Maturation of phagocytes                         | 0.000000133 |
| Activation of mveloid cells                      | 0.000000142 |
| Dermatitis                                       | 0.000000184 |
| Cellular infiltration                            | 0.000000209 |
| Enteritis                                        | 0.000000236 |

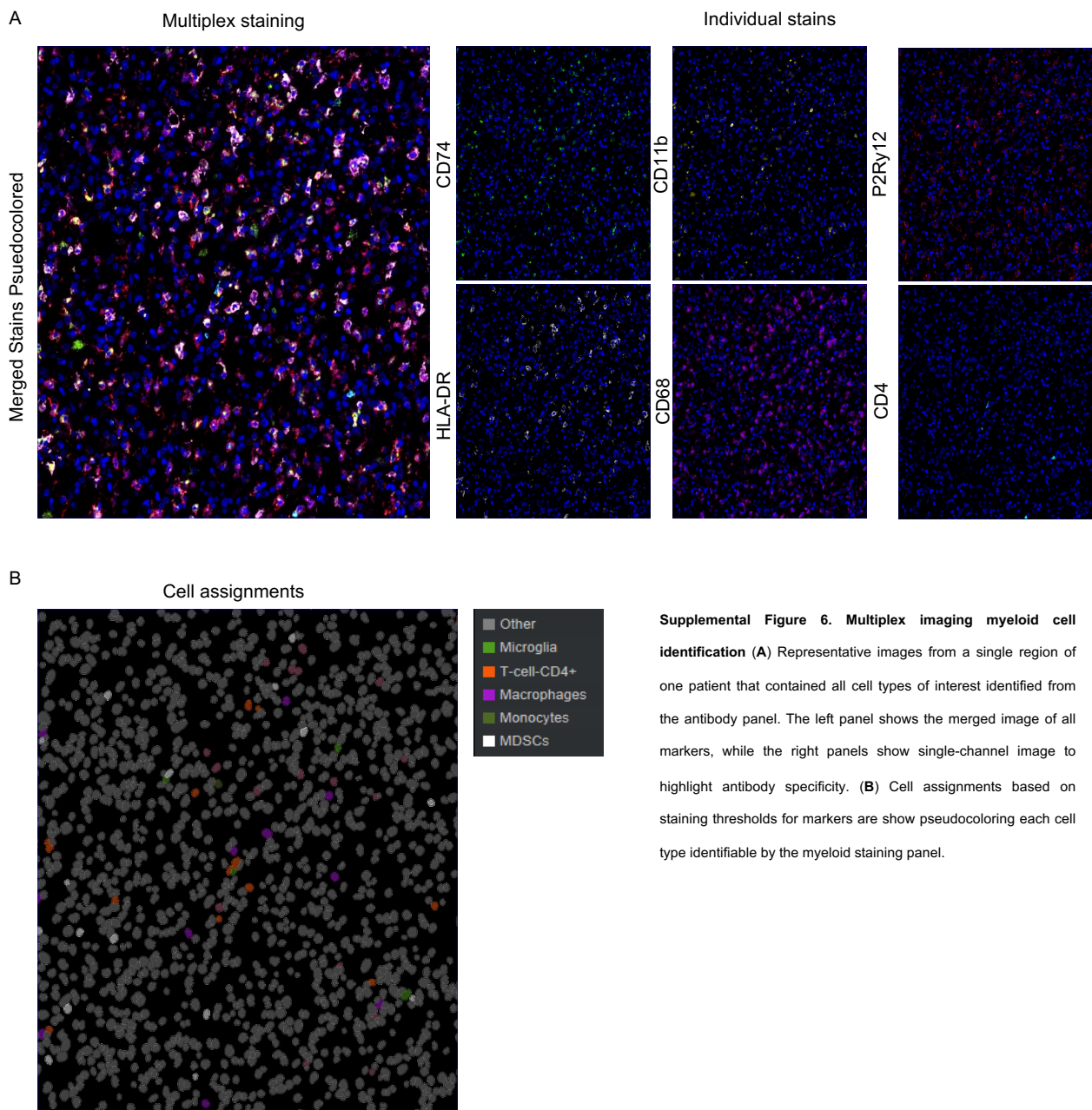
B

IPA Analysis top 100 Genes (G/G)

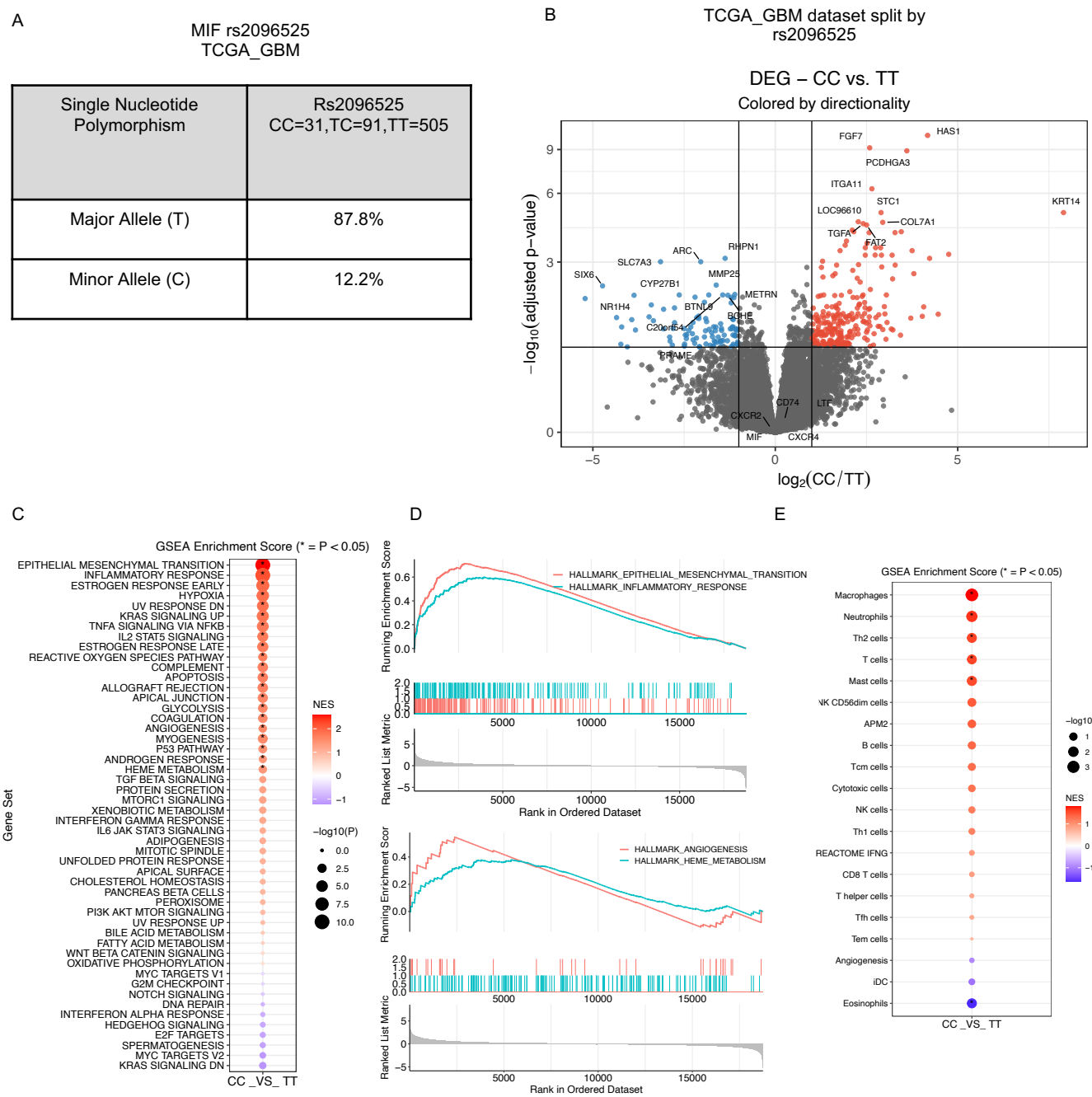
| Diseases or Functions Annotation                | p-value    |
|-------------------------------------------------|------------|
| Hair/nail type ectodermal dysplasia type 4      | 0.00000855 |
| Abnormal morphology of head                     | 0.0000124  |
| Morphology of head                              | 0.0000125  |
| Metabolism of histamine                         | 0.0000256  |
| Efflux of Ca2+                                  | 0.0000415  |
| Development of interneurons                     | 0.0000415  |
| Cleft palate                                    | 0.0000442  |
| Quantity of histamine                           | 0.000076   |
| Differentiation of lactotropes                  | 0.0000851  |
| Specification of neurons                        | 0.0000938  |
| Morphology of mouth                             | 0.000201   |
| Morphology of tongue                            | 0.000207   |
| Intercellular communication                     | 0.000234   |
| Morphology of posterior horn of the spinal cord | 0.000237   |
| Development of endocrine gland                  | 0.000251   |
| Abnormal morphology of central nervous system   | 0.00026    |
| Morphology of central nervous system            | 0.00027    |
| Abnormal morphology of nervous system           | 0.000281   |
| Tachycardia                                     | 0.00036    |
| Size of tongue                                  | 0.000379   |
| Differentiation of nervous system               | 0.000397   |
| Abnormal morphology of interneurons             | 0.000409   |
| Development of jaw bone                         | 0.000462   |
| Differentiation of neurons                      | 0.000462   |
| Morphology of nervous system                    | 0.000475   |

**Supplemental Figure 5. Ingenuity pathway analysis of C/G vs homozygous dominant rs755622.** Genes from the differential expression analysis of rs755622 minor allele vs major allele patients were ranked by log fold-change, and the top 100 genes increased with the minor allele and the top 100 decreased with the minor allele were subjected to Ingenuity Pathway Analysis. (A-B) Pathway description and p-value are shown for the top 25 pathways associated with the 100 genes.





Supplemental Figure 7- TCGA\_GBM analysis of the MIF SNP rs2096525 identifies increased immune signaling



**Supplemental Figure 7. TCGA\_GBM analysis of the MIF SNP rs2096525 identifies increased immune signaling.** (A) Analysis of TCGA\_GBM whole-exome sequencing for rs2096525 identified 12.2% of patients with the minor allele. (B) The TCGA\_GBM mRNA sequencing data and genotype information obtained from the whole-exome sequencing data (n=159) were used for differential expression analysis between patients with the minor allele (n=10) and patients homozygous for the major allele (n=113). Volcano plot represents deseq2 analysis of differential expression between the patients with the rs2096525 minor allele and patients homozygous for the major allele. (red = >1 log2FC & > 1 -log10 adjusted p-value, blue = <-1 log2FC & > 1 -log10 adjusted p-value) (C) GSEA analysis of Hallmark pathways from differential expression analysis of patients demonstrates increased pathways in rs2096525 SNP-containing patients. (D) Selected enriched top two pathways are shown for GSEA analysis, with ranked genes in each pathway for enrichment; the top two downregulated pathways also shown. (E) Pre-ranked gene lists of differential expression were utilized with the gene sets previously used for ssGSEA cell-type deconvolution. Deconvolution demonstrating an overall increase in macrophages, neutrophils, and T cell populations in samples from patients with the minor allele rs2096525 SNP.



**Supplemental Figure 8. GTEx database analysis of *MIF* and rs755622 as expression quantitative loci across tissues.** Searching the GTEx database for rs755622 and its association across multiple tissues for a link with *MIF* expression shows significance in many tissues except central nervous system-related tissues.