**Acute Inflammatory Response Following Increased Blood-Brain Barrier Permeability Induced by Focused Ultrasound is Dependent on Microbubble Dose**

Dallan McMahon and Kullervo Hynynen

**Supplementary Material**

**Supplementary Table 1:** Log2 fold change in gene expression relative to control region 6 hrs post-FUS and corresponding repeated measures, one-way ANOVA p-values

| Gene Names | Log2 Fold Change vs Control Region | ANOVA P-Value |
|------------|-----------------------------------|---------------|
|            | Scheme 1 | Scheme 2 | Scheme 3 |               |
| Agt        | -0.85    | 0.48     | -0.16    | 0.648         |
| Akt1       | -0.02    | 0.32     | -0.08    | 0.53          |
| Atf1       | 0.16     | 1        | 0.62     | 0.388         |
| Atf2       | 1.05     | 1.32     | 1.15     | 0.397         |
| Bcl10      | 0.12     | 0.86     | 0.59     | 0.21          |
| Bcl2a1     | 0.54     | 2.42     | 1.4      | 0.105         |
| Bcl2l1     | 0.3      | 0.63     | 0.3      | 0.776         |
| Bcl3       | -0.1     | 1.77     | 1.78     | 0.012         |
| Birc3      | 0.82     | 3.82     | 3.65     | 0             |
| Card10     | -0.78    | 0.29     | -0.81    | 0.012         |
| Card11     | -0.37    | 0.34     | -0.23    | 0.3           |
| Casp1      | 0.16     | 1.22     | 0.75     | 0.703         |
| Casp8      | -0.32    | 0.8      | 0.42     | 0.3           |
| Ccl2       | 1.94     | 5.73     | 5.44     | 0.014         |
| Ccl5       | -0.1     | 2        | 1.77     | 0.166         |
| Cdl40      | 0.29     | 1.87     | 1.72     | 0.026         |
| Cflar      | 0.3      | 0.9      | 0.63     | 0.089         |
| Chuk       | 0.1      | 0.66     | 0.33     | 0.739         |
| Crebbp     | 0.21     | 0.32     | 0.33     | 0.45          |
| Csf1       | -0.1     | 1.3      | 0.76     | 0.155         |
| Csf2       | -0.46    | 0.53     | -0.49    | 0.275         |
| Csf3       | -0.46    | 1.29     | -0.49    | 0.275         |
| Egfr       | -0.34    | 0.51     | 0.02     | 0.355         |
| Egr1       | 1.26     | 1.32     | 0.81     | 0.394         |
| Elf2ak2    | 0.08     | 0.46     | 0.3      | 0.939         |
| F2r        | 0.16     | 0.61     | 0.07     | 0.607         |
| Fadd       | 0.12     | 0.64     | 0.27     | 0.899         |
| Faslg      | 0.04     | 0.76     | 0.37     | 0.703         |
| Fos        | 0.74     | 2.35     | 2.16     | 0.041         |
| Hmox1      | 0.09     | 2.51     | 1.54     | 0.169         |
| Icam1      | 0.66     | 2.64     | 2.15     | 0.017         |
| gene      | row1 | row2 | row3 | row4 |
|-----------|------|------|------|------|
| Ifna1     | -0.45| 0.08 | -0.46| 0.308|
| Ifng      | -0.46| 0.08 | -0.49| 0.308|
| Ikbkb     | 0.11 | 0.61 | 0.21 | 0.896|
| Ikbke     | 0.03 | 0.12 | -0.12| 0.925|
| Ikbkg     | 0.04 | 0.6  | 0.19 | 0.97 |
| II10      | -0.46| 0.37 | -0.49| 0.234|
| II1a      | -0.42| 1.98 | 0.77 | 0.447|
| II1b      | 0.63 | 4.36 | 3.53 | 0.024|
| II1r1     | -0.47| 0.69 | 0.04 | 0.503|
| Irak1     | -0.02| 0.38 | 0.06 | 0.741|
| Irak2     | 0.23 | 1.17 | 0.66 | 0.205|
| Irak4     | -0.1 | 0.34 | -0.09| 0.944|
| Irf1      | 0.32 | 1.78 | 1.62 | 0.001|
| Jun       | -0.1 | 0.74 | 0.7  | 0.734|
| LOC687813 | -1.24| 0.22 | -0.83| 0.172|
| Lta       | 0.02 | 0.34 | -0.48| 0.435|
| Ltbr      | 0.12 | 1.11 | 0.87 | 0.335|
| Map2k3    | 0.97 | 2.14 | 1.76 | 0.16 |
| Map3k1    | 0.01 | 0.99 | 0.5  | 0.445|
| Mapk3     | -0.16| 0.33 | 0.26 | 0.576|
| Myd88     | 0.02 | 0.8  | 0.41 | 0.296|
| Nfkbi     | 0.18 | 1.01 | 0.75 | 0.123|
| Nkb2      | 0.17 | 2.04 | 1.49 | 0.023|
| Nfkbia    | 0.16 | 1.17 | 0.62 | 0.19 |
| Kat2b     | 0.11 | 0.76 | 0.32 | 0.732|
| Psip1     | 0.28 | 0.39 | 0.24 | 0.433|
| Raf1      | 0.22 | 0.56 | 0.43 | 0.492|
| Rel       | 0.62 | 1.29 | 0.96 | 0.093|
| Rela      | 0.1  | 1    | 0.62 | 0.19 |
| Ripk1     | 0.08 | 0.58 | -0.84| 0.47 |
| Ripk2     | 0.14 | 0.93 | -0.26| 0.169|
| Smad4     | 0.06 | 0.57 | 0.25 | 0.971|
| Stat1     | -0.03| 0.43 | 0.13 | 0.673|
| Tbk1      | 0.45 | 0.74 | 0.53 | 0.358|
| Timp1     | 0.49 | 3.31 | 2.79 | 0.046|
| Tlr1      | -0.43| 2.21 | 1.9  | 0.004|
| Tlr2      | 0.58 | 1.6  | 1.32 | 0.265|
| Tlr3      | -0.52| 0.6  | 0.01 | 0.401|
| Tlr4      | -0.41| -0.74| -0.77| 0.267|
| Tlr6      | -0.3 | 0.97 | 0.62 | 0.363|
| Tlr9      | -0.33| 0.46 | -0.45| 0.144|
| Tnf       | 0.9  | 4.03 | 3.17 | 0.002|
| Gene Names | Log2 Fold Change vs Control Region | ANOVA P-Value |
|------------|----------------------------------|---------------|
| Tnfrsf10b  | -0.75 | 0.69 | -0.06 | 0.309 |
| Tnfrsf1a   | 0.87 | 2.19 | 1.54 | 0.213 |
| Tnfrsf1b   | -0.7 | 1.47 | 0.43 | 0.142 |
| Tnfsf10    | -0.11 | 0.07 | -0.38 | 0.607 |
| Tnfrsf14   | -0.46 | 0.08 | -0.22 | 0.599 |
| Tollip      | 1.07 | 1.27 | 1.53 | 0.192 |
| Tradd       | -0.09 | 0.52 | -0.26 | 0.972 |
| Traf2       | 0.08 | 0.64 | 0.26 | 0.989 |
| Traf3       | 0.06 | -0.01 | -0.04 | 0.489 |
| Traf6       | 0.06 | 0.55 | 0.33 | 0.666 |
| Zap70       | -0.36 | 0.08 | -0.49 | 0.5 |

**Supplementary Table 2:** Log2 fold change in gene expression relative to control region 4 Days post-FUS and corresponding repeated measures, one-way ANOVA p-values

| Gene Names | Log2 Fold Change vs Control Region | Scheme 1 | Scheme 2 | Scheme 3 | ANOVA P-Value |
|------------|----------------------------------|---------|---------|---------|---------------|
| Agt        | -0.62 | -0.34 | -0.27 | 0.665 |
| Akt1       | 0.1 | 0.11 | 0.31 | 0.228 |
| Atf1       | 0.34 | 0.11 | 0.28 | 0.016 |
| Atf2       | 0.35 | 0.05 | 0.17 | 0.653 |
| Bcl10      | 0.16 | 0.58 | 0.24 | 0.193 |
| Bcl2a1     | 0.94 | 1.73 | 1.95 | 0.407 |
| Bcl2l1     | -0.35 | 0.38 | 0.54 | 0.618 |
| Bcl3       | 0.39 | 0.41 | 1.13 | 0.858 |
| Birc3      | 1.3 | 0.58 | 1.91 | 0.892 |
| Card10     | -0.6 | 0.26 | -0.37 | 0.307 |
| Card11     | 0.24 | 1.02 | 0.18 | 0.674 |
| Casp1      | -0.04 | 0.86 | 0 | 0.6 |
| Casp8      | 1.53 | 1.66 | 1.89 | 0.498 |
| Cd2        | -0.51 | 1.27 | -0.12 | 0.042 |
| Cd5        | -0.67 | 0.01 | -0.23 | 0.785 |
| Cd40       | -0.13 | 0.9 | -0.17 | 0.74 |
| Cflar      | 0.16 | -0.15 | -0.01 | 0.358 |
| Chuk       | 0.22 | 0.13 | 0.86 | 0.628 |
| Crebbp     | 1.5 | -0.11 | 1.4 | 0.025 |
| Csf1       | 0.46 | 0.88 | 0.72 | 0.124 |
| Csf2       | -1.31 | 0.28 | -0.5 | 0.632 |
| Csf3       | -0.24 | -0.27 | 0.12 | 0.652 |
| Egrf       | 0.17 | -0.31 | 0.46 | 0.292 |
| Egr1       | 1.75 | 0.87 | 2.12 | 0.216 |
| Elf2ak2    | -0.12 | 0.28 | -0.14 | 0.623 |
| F2r        | -0.19 | 1.15 | 0.28 | 0.842 |
| Gene     | Value1 | Value2 | Value3 | Value4 |
|----------|--------|--------|--------|--------|
| Fadd     | 0.15   | 0.56   | 1.05   | 0.3    |
| Faslg    | -0.43  | -0.43  | -0.31  | 0.769  |
| Fos      | 0.36   | 0.52   | 0.52   | 0.832  |
| Hmox1    | 0.58   | 1.5    | 0.9    | 0.813  |
| Icam1    | -0.62  | 1.15   | -0.07  | 0.308  |
| Ifna1    | 0.63   | 0.26   | 0.93   | 0.754  |
| Ifng     | 0.03   | 0.06   | 0.41   | 0.754  |
| Ikkb     | -0.24  | 0.5    | 0.05   | 0.849  |
| Ikkbe    | -1.03  | 0.65   | -0.44  | 0.339  |
| Ikkbg    | 1.33   | 0.01   | 1.39   | 0.895  |
| Il10     | 1.21   | -0.27  | 1.87   | 0.652  |
| Il1a     | -0.68  | 0.1    | -0.15  | 0.744  |
| Il1b     | -0.36  | 0.61   | 0.65   | 0.515  |
| Il1r1    | -0.42  | 0.56   | 0.11   | 0.263  |
| Irak1    | 0.04   | -0.05  | 0.15   | 0.327  |
| Irak2    | -0.04  | -0.11  | -0.52  | 0.345  |
| Irak4    | -0.13  | 0.42   | -0.5   | 0.159  |
| Irf1     | 0.92   | 0.21   | 1.21   | 0.836  |
| Jun      | -0.6   | 0.52   | 0.02   | 0.268  |
| LOC687813| -0.17  | 0.57   | 0.65   | 0.84   |
| Lta      | 0.08   | 0.2    | 1.14   | 0.749  |
| Ltbr     | 1.43   | 0.89   | 1.57   | 0.823  |
| Map2k3   | 0.46   | 0.26   | 1.14   | 0.448  |
| Map3k1   | -0.06  | 0.59   | 0.16   | 0.858  |
| Mapk3    | -0.03  | 0.39   | 0.59   | 0.129  |
| Myd88    | -0.07  | 0.02   | -0.15  | 0.931  |
| Nkb1     | -0.11  | 0.06   | 0.2    | 0.648  |
| Nkb2     | -1.64  | 0.23   | -1.15  | 0.63   |
| Nkbia    | -1.02  | 0.16   | -0.8   | 0.522  |
| Kat2b    | 0.8    | 0.39   | 0.95   | 0.339  |
| Psip1    | 0.24   | 0.29   | 0.36   | 0.625  |
| Raf1     | 1.45   | 0.17   | 1.26   | 0.027  |
| Rel      | -0.5   | 0.69   | -0.18  | 0.429  |
| Rela     | 0.64   | 0.8    | 0.81   | 0.993  |
| Ripk1    | 0.59   | 0.31   | 1.27   | 0.091  |
| Ripk2    | -0.12  | 0.94   | 0.19   | 0.858  |
| Smad4    | 0.12   | 0.48   | 0.55   | 0.48   |
| Stat1    | -0.25  | 0.62   | 0.38   | 0.289  |
| Tbk1     | 0.24   | 0.44   | 0.37   | 0.364  |
| Timp1    | 0.52   | 2.4    | 1.2    | 0.035  |
| Tlr1     | 0.23   | 1.54   | 0.76   | 0.221  |
| Tlr2     | 0.32   | 1.38   | 0.52   | 0.489  |
| Gene   | Value1 | Value2 | Value3 | Value4 |
|--------|--------|--------|--------|--------|
| Tlr3   | 1.08   | 1.33   | 1.17   | 0.404  |
| Tlr4   | 0.92   | 0.74   | 0.57   | 0.634  |
| Tlr6   | -0.32  | 0.51   | -0.4   | 0.522  |
| Tlr9   | 0.12   | 1.32   | 0.31   | 0.729  |
| Tnf    | -0.2   | 0.03   | 0.81   | 0.91   |
| Tnfrsf10b | -0.64 | -0.03 | -0.25 | 0.583 |
| Tnfrsf1a | -0.42 | 0.18  | 0.03   | 0.786  |
| Tnfrsf1b | 0.14  | 1.1    | 0.51   | 0.696  |
| Tnfsf10 | -0.79  | -0.13  | 0.08   | 0.16   |
| Tnfsf14 | -1.84  | 0.01   | -1.17  | 0.632  |
| Tollip | 0.3    | 0.26   | 0.2    | 0.744  |
| Tradd  | -1.56  | -0.05  | -1.5   | 0.398  |
| Traf2  | 0.06   | -0.32  | 0.78   | 0.202  |
| Traf3  | 1.09   | -0.03  | 1.59   | 0.222  |
| Traf6  | -0.38  | 0.34   | 0.08   | 0.985  |
| Zap70  | 0.04   | 0.23   | 0.76   | 0.749  |