Ah receptor antagonism attenuates growth factor expression, proliferation and migration in fibroblast-like synoviocytes from rheumatoid arthritis patients.

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Supplementary Figure 1. Genomic sequences spanning the indicated regions for human epiregulin (EREG), amphiregulin (AREG) and vascular endothelial growth factor A (VEGFA) were obtained from the NCBI gene database. Putative dioxin response elements (DREs), which match the consensus sequence are highlighted in green, while those which deviate from the consensus sequence are highlighted in red. Deviations from the consensus DRE sequence are marked as lowercase. The core invariant region is underlined.

Human EREG -1996/-160 Sequence

-1996

AGCACTAACTCGGTACTAGGCACTCTACTAAGCACTTTCATTATTTTCCTATGCGCTGGATACTATTATTATCCCTG
TTTTACGTATGAGGAAATTGAGACAGATTAAATAACTTGTCCAGGAATTCACACACAGACAGTTTAAATCTTAACCC
CTGATAACATGATGAAGTATTTGTTTCTTTTTTTTTTTTTTTTGAGACGGAGTTTCGCTCTGTCGCCCAGGCTGGAG
TGCAGTGGCGCGATCTCGACTCACTGCAAGCTCCGCCTCCCGGgtTCACGCCATTCTCCTGCCTCAGCCTCCCGTGT
AGCTGGGACTACAGGCGCGCGCCACCATGCCCGGCTAATTTTTGTATTTTTAGTAGAGACGGGGTTTCACTGTGTTA
TCCAGGATGGTCTCGATCTCCTGAcCTCGTGATccGCTCGTCTCGGCCTCCCAAAGTGCTGGGATTACaGGCGTGAG
ccACCGCGCCCGGCCGAAGTATTTGTTTCTAACAAGAGCATTCTGGACATTAAAGGGCCTTAGAGTATGAGAGAAAA
AAGCCAGAAAAAAAAAAGGAATAGTAATAATAATTTTTTAAAAAGTAGAAATAAAAAGGTAAGGAGTTAACATCCAT
TAGATTCCATTTTCTATTCAAATATGTATATTTACATACAGTACTGCTGAATTGACTCACAGTTCTTAGGTCCTATA
GAGGAGTGCAGTGAAAAGGAAGACAATTTACACAGTACAGAGCTGAACATAGGACTTACAAACAAAAAAAAAGTCAA
GGAATACAAAGTAGCTTTCCCAGGTGTAAAGTACCGGGTCTAGAATTCTATGAGGCTAGGGAGAAGATAAACGACAA
AAGCTATAAGAGATCAGAATGAAAAGAGATCCACAAGCCTAAGAAGCCCAGGCCCTTGAGGAGAACCATGAATTTGA
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AGTGAGGAAAGGCTTAGAGTTTTCCAGCCTGGCTGGGGTCAGACAATTTGCCTGGGGAAATAGTGGGAGCTGAGGTT
GAAAAGACCGATTGGCTTCACGTTTGTGGCAGGCCTTGTCCAAAAAGCAATAGGAAGTCGTTGAAAGGTTTTGTGCA
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AATCACTGACAGACTTCAAGTTAAGGGAGTTTTCGTGgcTGAGGTTAGTAAgTCaCACGCACAGCTCTCCAAAGGCA
TGTATGGGGAACGCCAGCCTTGGCTAAAAGACTGATTCAAGTTATGTCCGTCACCCTGAGCAACCAAAACCACCCAC
TACAGGGCAGGTGACCCCACAAAGCAAACCAAGCCATCTGGTCCACGCTCCCCACCTCCCGGAGGGAGATGGAAAAG
TTTCGGGAGTAGTCCCCGGCCAATCGGAAAGACATTTTTTCATTCCTCAACCAC-160

Human VEGFA -2010/+1043 Sequence

-2010

AGAGGCGCACAAGGAGGAAAGTTAGTGGCTTCCCTTCCATATCCCGTTCATCAGCCTAGAGCATGGAGCC
CAGGTGAGGAGGCCTGCCTGGGAGGGGGCCCTGAGCCAGGAAATAAACATTTACTAACTGTACAAAGACC
TTGTCCCTGCTGCTGGGGAGCCTGCCAAGTGGTGGAGACAGGACTAGTG**CACG**AATGATGGAAAGGGAGG
GTTGGGGTGGGTGGGAGCCAGCCCTTTTCCTCATAAGGGCCTTAGGACACCATACCGATGGAACTGGGGG
TACTGGGGAGGTAACCTAGCACCTCCACCAAACCACAGCAACATGTGCTGAGGATGGGGCTGACTAGGTA
AGCTCCCTGGAGCGTTTTGGTTAAATTGAGGGAAATTGCTGCATTCCCATTCTCAGTCCATGCCTCCACA
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CAGCTGGCCTACAGACGTTCCTTAGTGCTGGCGGGTAGGTTTGAA**TcATCACGCAg**GCCCTGGCCTCCAC
CCGCCCCCACCAGCCCCCTGGCCTCAGTTCCCTGGCAACATCTGGGGTTGGGGGGGCAGCAGGAACAAGG
GCCTCTGTCTGCCCAGCTGCCTCCCCCTTTGGGTTTTGCCAGACTCCACAGTGC**aTaCGTGgGct**CCAAC
AGGTCCTCTTCCCTCCCAGTCACTGACTAACCCCGGAACCACACAGCTTCCCGTTCTCAGCTCCACAAAC
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ACACTGTGGCCCCTGTGCCCAGCCCTGGGCTCTCTGTACATGAAGCAACTCCAGTCCCAAATATGTAGCT
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TTTAGCCAGAGCCGGGGTGTGCAGACGGCAGTCACTAGGGGGCGCTCGGCCACCACAGGGAAGCTGGGTG
AATGGAGCGAGCAGCGTCTTCGAGAGTGA**GGaCGTGtGTG**TCTGTGTGGGTGAGTGAGTG**TGTGCGTGtG**
gGGTTGAGGGCGTTGGAGCGGGGAGAAGGCCAGGGGTCACTCCAGGATTCCAATAGATCTGTGTGTCCCT
CTCCCCACCCGTCCCTGTCCGGCTCTCCGCCTTCCCCTGCCCCCTTCAATATTCCTAGCAAAGAGGGAAC
GGCTCTCAGGCCCTG**TcCGCACGtAA**CCTCACTTTCCTGCTCCCTCCTCGCCAATGCCCCGCGGGCGCGT
GTCTCTGGACAGAGTTTCCGGGGGCGGATGGGTAATTTTCAGGCTGTGAACCTTGGTGGGGGTCGAGCTT
CCCCTTCATTGCGGCGGGCTGCGGGCCAGGCTTCACTGAGCGTCCGCAGAGCCCGGGCCCGAGCCG**CGTG**
tGgAAGGGCTGAGGCTCGCCTGTCCCCGCCCCCCGGGGCGGGCCGGGGGCGGGGTCCCGGCGGGGCGGAG
CCATGCGCCCCCCCCTTTTTTTTTTAAAAGTCGGCTGGTAGCGGGGAGGATCGCGGAGGCTTGGGGCAGC
CGGGTAGCTCGGA**GGTCGTGgcgc**TGGGGGCTAGCACCAGCGCTCTGTCGGGAGGCGCAGCGGTTAGGTG
GACCGGTCAGCGGACTCACCGGCCAGGGCGCTCGGTGCTGGAATTTGATATTCATTGATCCGGGTTTTAT
CCCTCTTCTTTTTTCTTAAACATTTTTTTTTAAAACTGTATTGTTTCTCGTTTTAATTTATTTTTGCTTG
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CAGAGAGAGCGCGC**GGGCGTGCGAG**CAGCGAAAGCGACAGGGGCAAAGTGAGTGACCTGCTTTTGGGGGT
GACCGCCGGAGCG**cGGCGTGAGcc**CTCCCCCTTGGGATCCCGCAGCTGACCAGTCGCGCTGACGGACAGA
CAGACAGACACCGCCCCCAGCCCCAGCTACCACCTCCTCCCCGGCCGGCGGCGGACAGTGGACGCGGCGG
CGAGCCGCGGGCAGGGGCCGGAGCCCGCGCCCGGAGGCGGGGTGGAGGGGGTCGGGGCTCGCGGCGTCGC
ACTGAAACTTTTCGTCCAACTTCTGGGCTGTTCTCGCTTCGGAGG**aGcCGTGgTcc**GCGCGGGGGAAGCC

GAGCCGAGCGGAGCCGCGAGAAGTGCTAGCTCGGGCCGGGAGGAGCCGCAGCCGGAGGAGGGGGAGGAGG
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CGGGGAGGAAGAGTAGCTCGCCGAGGCGCCGAGGAGAGCGGGCCGCCCCACAGCCCGAGCCGGAGAGGGA
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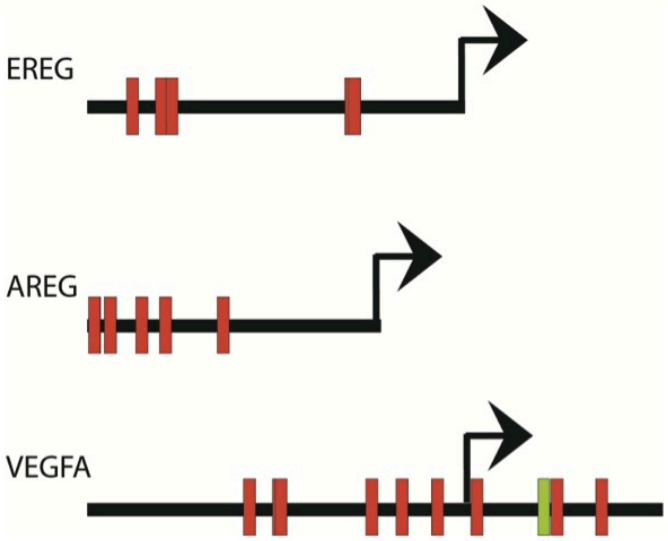
Positioning of putative DREs relative to the transcription start site



Supplementary figure 2. GNF351 inhibits cytokine-induced MMP-2 and -9 expression in primary fibroblast-like synoviocytes. RA-FLS were pretreated for 1 h with 500 nM GNF351 followed by a single administration of 10 ng/ml IL1B for 48 h. Cells were then treated every 12 h with 500 nM GNF351 for a total of 48 h. Cell culture supernatants were collected and a gelatin zymography was performed.