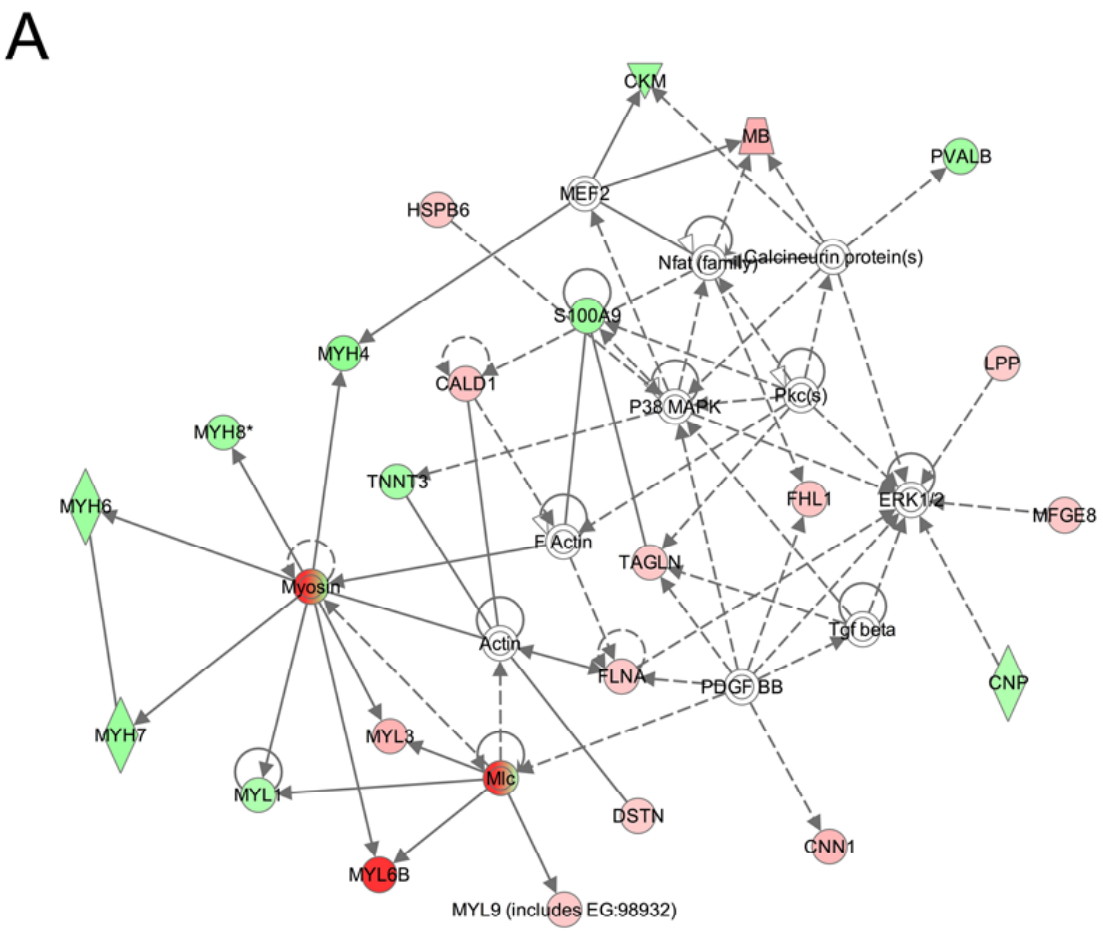
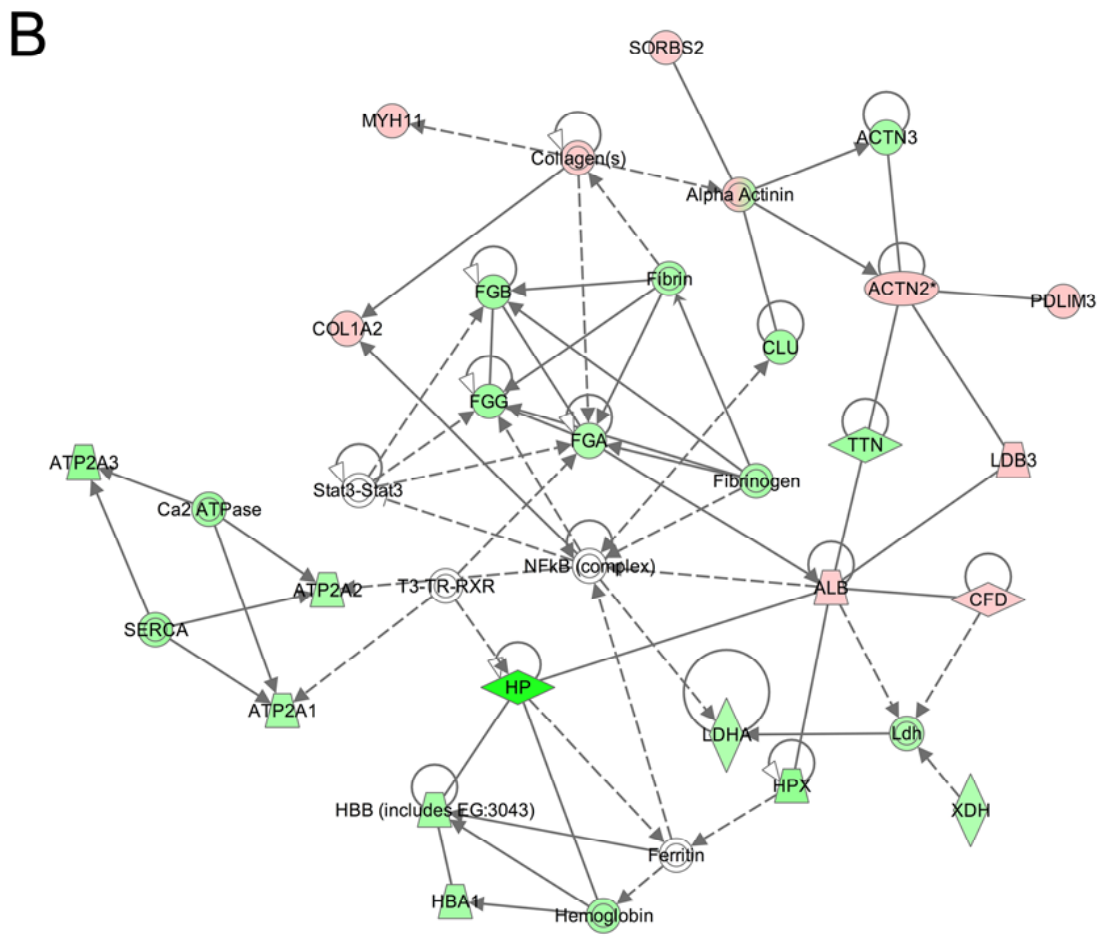
Comley et al – Supplementary Figure 3





Supplementary figure 3. Systems level analysis reveals potential apoE genotype-dependent modification of protein interaction pathways in uninjured peripheral nerves. A: Ingenuity Pathway Analysis generated protein interaction network involved in regulation of tissue and cell morphology (based around interactions of myosin and actin proteins) modified in apoE4 uninjured peripheral nerves compared to apoE3 tissue (green = up in apoE4 vs apoE3; red = down in apoE4 vs apoE3; grey = unchanged). Solid connecting lines indicate the presence of a direct interaction and dashed connecting lines indicate an indirect interaction. B: Ingenuity Pathway Analysis generated protein interaction network involved in haematological regulation (including integrity of the blood-brain/blood-nerve barrier) modified in apoE4 uninjured peripheral nerves compared to apoE3 tissue (green = up in apoE4 vs apoE3; red = down in apoE4 vs apoE3; grey = unchanged). A: Actin; calcineurin proteins; CALD1 – h-caldesmon; CKM – muscle creatine kinase; CNN1 – h1-calponin alpha; CNP - 2',3'-

cyclic nucleotide 3' phosphodiesterase isoform 2; DSTN – destrin isoform CRA_b; ERK1/2 – extracellular signal-regulated kinase; F Actin – filamentous actin; FHL1 - skeletal muscle LIM protein; FLNA - filamin alpha; HSPB6 - heat shock protein, alpha-crystallin-related, B6; LPP - LIM domain containing preferred translocation partner in lipoma isoform 1; MB – myoglobin; MEF2 – myocyte enhancer factor 2; MFGE8 - milk fat globule-EGF factor 8 protein isoform 2; MLC - mKIAA0777 protein; MYH4 - myosin, heavy polypeptide 4, skeletal muscle; MYH6 - alpha cardiac myosin heavy chain; MYH7 - Myh7 protein; MYH8 - myosin, heavy polypeptide 8, skeletal muscle, perinatal; MYL1 - fast skeletal myosin alkali light chain 1 isoform 1f; MYL3 - myosin, light polypeptide 3, isoform CRA_a; MYL6B - myosin, light polypeptide 6B; MYL9 (includes EG:98932) - myosin regulatory light polypeptide 9; Myosin - Myosin-binding protein C, fast-type; Nfat family – nuclear factor of activated T-cells; P38 MAPK - P38 mitogen-activated kinase; PDGF BB – platelet-derived growth factor beta polypeptide; Pkc(s) – protein kinase C; PVABL – parvalbumin; S100A9 - S100 calcium binding protein A9 (calgranulin B); TAGLN – transgelin; Tgf beta – transforming growth factor beta; TNNT3 - troponin T. B: ACTN2* - actinin alpha 2; ACTN3 - actinin alpha 3; ALB - albumin precursor; Alpha Actinin - Actinin alpha 2; ATP2A1 - ATPase, Ca++ transporting, cardiac muscle, fast twitch 1, isoform CRA_c; ATP2A2 - ATPase, Ca++ transporting, slow twitch 2 isoform a; ATP2A3 (aka SERCA); Ca2 ATPase – ATPase, Ca++ transporting, ubiquitous; CFD - adipsin precursor; CLU - clusterin precursor; COL1A2 - procollagen, type I, alpha 2 precursor; Collagen(s) - Collagen alpha-1(XIV) chain; Ferritin; FGA - fibrinogen, alpha polypeptide, isoform CRA_b; FGB - fibrinogen beta chain precursor; FGG - fibrinogen, gamma polypeptide; Fibrin; Fibrinogen; HBA1 - haemoglobin alpha, adult chain 2; HBB (includes EG:3043) - haemoglobin, beta adult major chain; Haemoglobin; HP - haptoglobin precursor; HPX - hemopexin precursor; LDB3 - LIM domain binding 3 isoform b; Ldh - lactate dehydrogenase; LDHA - lactate dehydrogenase A isoform 1; MYH11 - myosin, heavy chain 11, smooth muscle; NFkB (complex) - nuclear factor of kappa light polypeptide gene enhancer in B-cells; PDLIM3 - PDZ and LIM domain protein 3; SERCA – (aka ATP2A3); SORBS2 - mKIAA0777 protein; Stat3-Stat3 - signal transducer and

activator of transcription 3; T3-TR-RXR – thyroid hormone receptor/retinoid X receptor heterodimer; TTN – titin; XDH - xanthine dehydrogenase.