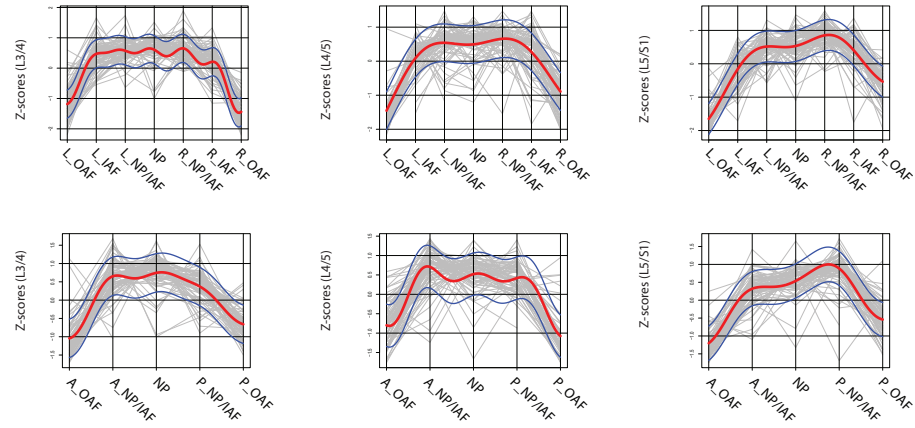


A

Proteins in Y1 (n=96):

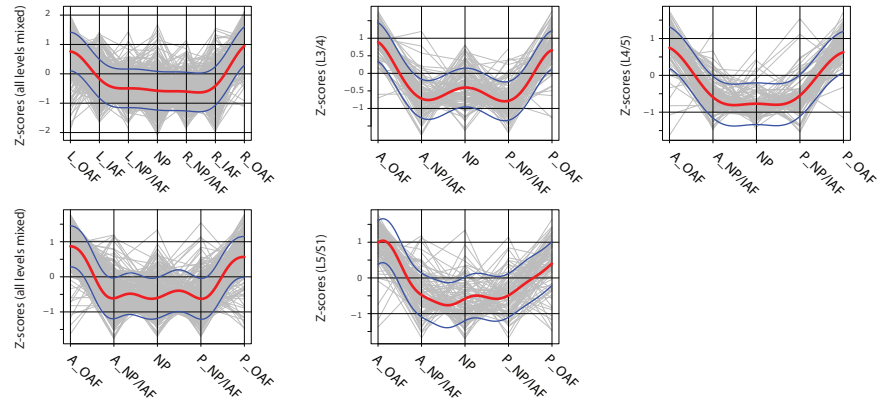
DAG1, DNAJC3, FIBIN, LPL, NUCB1, CPQ, GARS, PREP, RSU1, CLEC3B, EFEMP1, KRT19, FN1, PRG4, CXCL12, B4GAT1, KAL1, CSPG4, INHBA, SLIT3, **CDH1**, SLPI, CYTL1, IGFBP5, CHAD1, ISLR, COL5A2, MATN3, EFHD2, VIT, SMOCC2, PCOLCE2, BCAN, CST3, CCDC80, ATRN, EMILIN1, EPHX1, RNASE4, PCOLCE, COL11A2, OAF, PLOD1, XYL1, DKK3, CLSTN1, EDIL3, MFI2, COL5A1, SERPINA5, C1S, CP, SERPING1, FRZB, APOD, COL11A1, TXNRD1, IL17B, QSOX1, SERPINE2, TNFRSF11B, MXRA5, PDGFRL, **CD109**, KRT8, SEMA3C, TIMP3, CFB, HYAL1, ITIH5, SMOCC1, PXLYP1, COL3A1, THBS3, VAPA, GALNT2, CCT4, **MECP2**, GDF6, CHRDL2, UBXN10, TIMP1, PDGFC, IGFBP7, CYFIP1, SLC44A2, PPP2R1A, SEPP1, AKR1C1, MGAT1, VEGFA, GBA, RPL6, ENPP2, SCUBE1



B

Proteins in Y2 (n=171):

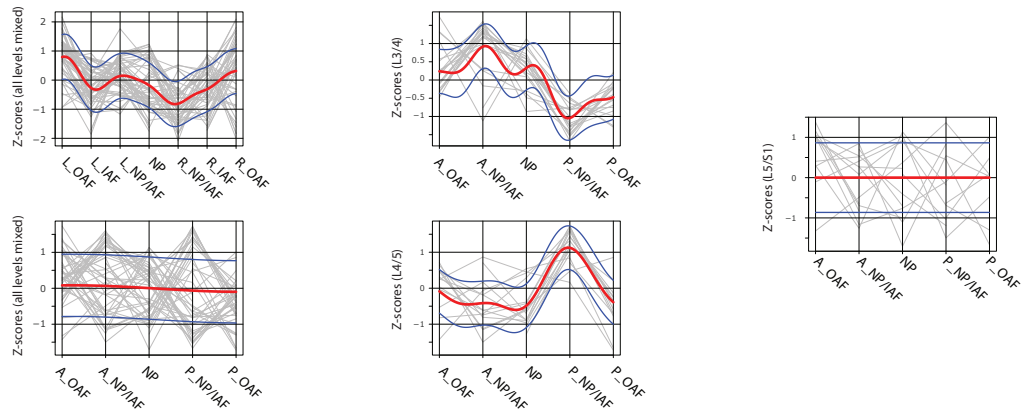
HSP90B1, **CD81**, GDI2, PGLS, RAB1A, KRT2, KRT9, RPS21, SDCBP, GOT1, HNRNP, F12, RAP1B, ARF4, ANXA4, ANXA6, DDOST, COMP, CILP, BGN, DSG1, OGN, PRELP, GNAI2, ANXA5, PKM, TFG, SRPX2, DCN, LUM, NES, ANXA7, H2AFV, ANXA1, GSTP1, CTSD, BPGM, YWHAQ, F11, SOD1, PRDX2, F13A1, CAT, IGHV5-51, SKP1, APEX1, **HIST1H1B**, CTSG, APOC3, TUBB, HBA1, CA2, SELENBP1, CA1, HBG1, TAGLN, ACTG1, CLIC1, HSP90AA1, SERPINB1, YWHAZ, CFL1, HIST1H4A, HBD, HBB, SERPINA7, SPARC, AK1, GPI, RPS27A, COL1A1, LAMA2, DPYSL3, IDH2, COL4A2, HSPB1, HUWE1, SH3BGR1, ATP5A1, ATP5B, HIST2H2AC, AOC2, CILP2, DEFA3, GAPDH, MPZ, MSN, LOX, EIF4A1, APO1, SERPINB6, RPL3, CAPZA2, UBA1, ASPN, MMP3, RPS8, ARF1, IGKV4-1, RPL18, **NTSE**, ACTN1, CAP1, CALM3, HSPA1B, HSPA8, C4A, YWHA, SDHA, VWA1, COL6A2, COL6A1, COL6A3, FMOD, HNRNP2B1, COL12A1, COL14A1, AHNK, LMNA, AMBP, SERPINF1, LAMC1, ITIH1, LAMB2, NID1, THBS4, THBS1, THBS2, MYH9, PLS3, CALR, PFN1, SND1, HIST1H2BL, HNRNP1, MYL6, MYL12A, SERPINH1, PDIA3, ANXA2, RPS3, NCL, PPIA, VCP, XRCC6, FSCN1, IQGAP1, CYBR3, TAGLN2, PDIA6, FBLN1, MFGE8, TGFBI, CFD, MAMDC2, MATN2, LMNB2, LAMA4, SPSN, DPYSL2, ACTN4, VAT1, FLNA, CDSN, SPTBN1, SPTAN1, TPM4, TUBA1B, VCL, ACO2, PAPPA



C

Proteins in Y3 (n=25):

ANGPTL7, RPN2, ALDOA, ENO3, CKM, CA3, MB, MYBPC1, MYL2, MYH2, TNNC1, ACTN2, MYH1, MYH7, MYLPF, MYL3, TPM2, TPM3, PYGM, TNNT3, TPM1, TPT1, ACLY, HHIP, NAP1L1



D

Proteins in Y4 (n=48):

RCN2, PGAM2, C8B, HP, APOA4, AKR1B1, C1QB, PGLYRP2, APOB, IGHM, SERPINF2, ITIH4, APCs, ITIH2, PLG, IGHG4, ITIH3, LBP, SERPINA4, C8G, C4BPA, PLIN4, IGHG3, IGLC6, C8A, GC, ORM1, C9, A1BG, HLA-DRB1, HSPD1, LRG1, F2, KNG1, ORM2, FGA, APOA1, FGB, FGG, IGHA1, HRG, HPX, TTR, VTN, IGHG1, ALB, IGHG2, TF

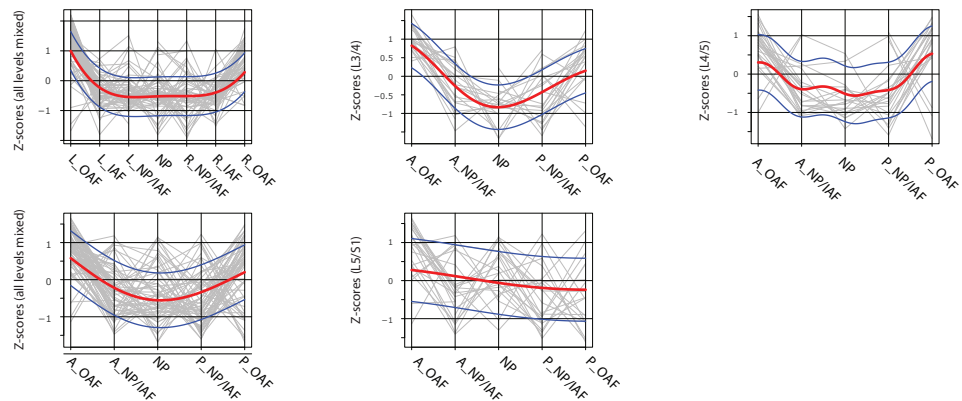


Figure 3—figure supplement 3. Modular trends along the lateral or anteroposterior axes in the young non-degenerated discs.

(A)–(D) Proteins in modules Y1 (A), Y2 (B), Y3 (C) and Y4 (D), and their directional trends, in the young profiles. The red curve is the Gaussian Process Estimation (GPE) trend line, and the blue curves are 1 standard deviation above or below the trend line. Genes in red are transcription factors or DNA binding proteins. Genes in blue are surface markers.