Gene expression in patients with abdominal aortic aneurysm - more than immunological mechanisms involved

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Introduction

Abdominal aortic aneurysm (AAA) is a serious condition of unclear pathogenesis and progression. Immunological mechanisms represent an important pathogenic factor involved in AAA development.

Aim of study

Our study compared gene expression in the tissue of AAA and in the healthy part of the proximal neck of the aorta in the same patient.

Patients and methodology

The total of 48 patients with AAA who required an open surgical procedure were included into the study Two samples were collected from each patient during AAA surgery. One sample was collected from the aneurysm, the other from the aneurysm proximal neck where the tissue did not exhibit any aneurysmal changes. Subsequently, gene expression profiles using microarrays (Illumina) were compared in RNA extracted from the samples.

Table 1. Differentially expressed genes with FDR < 0,05 and FC ≥ 2

SYMBOL	GENE NAME	logFC
ITGA8	integrin, alpha 8	-1.77
TCEAL2	transcription elongation factor A (SII)-like 2	-1.55
MRAP2	melanocortin 2 reeptor accessory protein 2	-1.49
HS3ST2	heparan sulfate (glucosamine) 3-O-sulfotransferase 2	-1.4
KCNA5	potassium channel, voltage gated shaker related subfamily A, member 5	-1.36
MRAP2	melanocortin 2 reeptor accessory protein 2	-1.32
CST6	cystalin E/M	-1.28
MYH11	myosin, heavy chain 11, smooth muscle	-1.28
PLN	phospholambam	-1.28
TREM1	triggering receptor expressed on myeloid cells 1	-1.28
LMOD1	leiomodin 1 (smooth muscle)	-1.27
CST6	cystalin E/M	-1.26
IGFBP2	Insulin-like growth factor binding protein 2, 36 kDa	-1.23
TM4SF19	transmembrane 4 L six family member 19	-1.22
NXPH3	neurexophilin 3	-1.21
PCDH7	protocadherin 7	-1.21
RGS5	regulator of G-protein signaling 5	-1.21
SHROOM 3	shroom family member 3	-1.21

Results

Overall, 2,185 genes were found to be upregulated and 2,100 downregulated; from which 158 genes had a different expression with FDR < 0.05 (False Discovery Rate) and FC ≥ 2 (Fold Change). Of this number, 115 genes were over-expressed and 43 under-expressed. The analysis of the gene list based on their biological pathways revealed that the regulation of inflammation was mediated by chemokine and cytokine signaling pathways, the integrin signaling pathway, and T and B cell activation. Moreover, a change was identified in the expression of genes involved in both intercellular and intracellular signaling systems.

Figure 1 . Heatmaps for 1000 of the most differently expressed genes

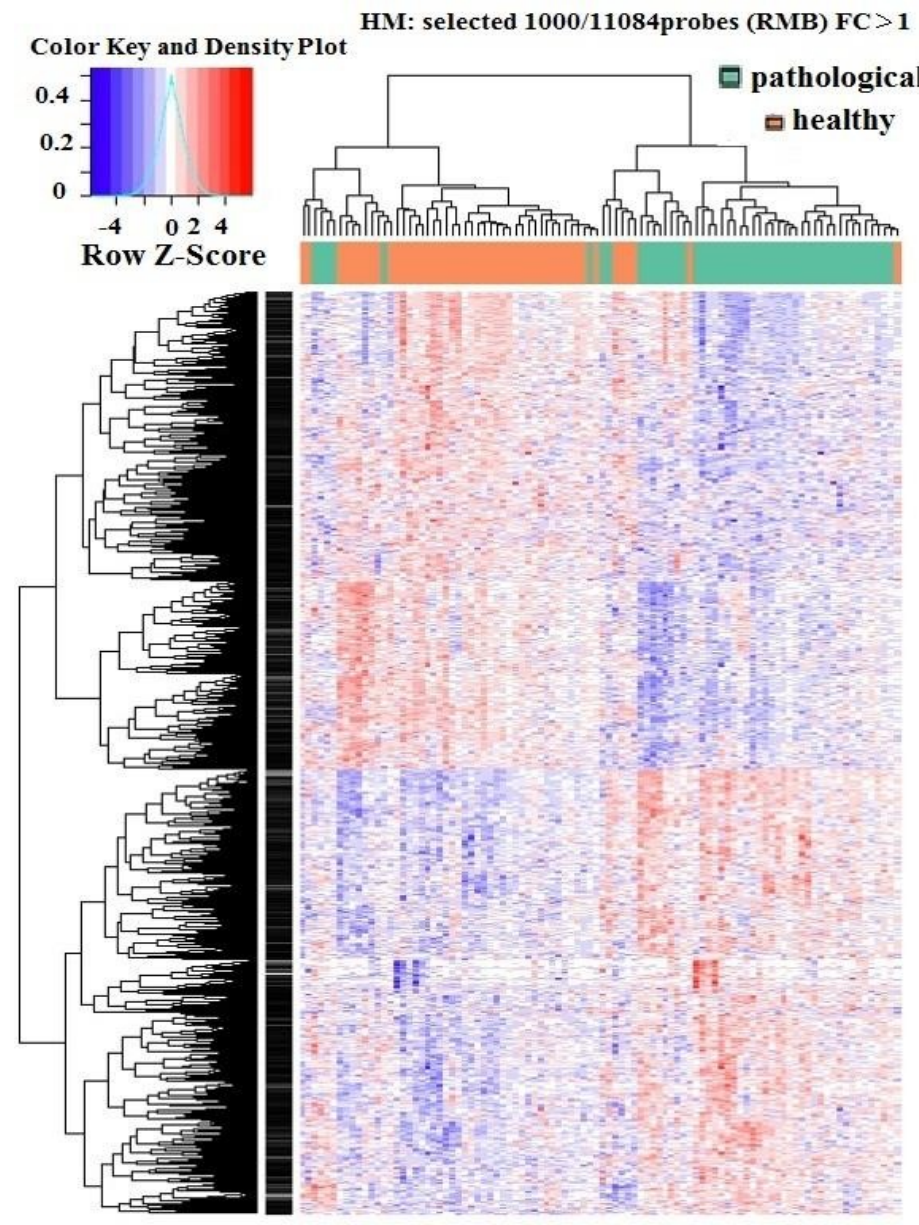

Table 2. Pathways related to the most differentially expressed genes

Name	Status
Dilated cardiomyopathy	activated
Chemokine signaling pathway	activated
Cytokine-cytokine receptor interaction	activated
Vascular smooth muscle contraction	activated
Leukocyte transendothelial migration	activated
NF-kappa B signaling pathway	activated
Calcium signaling pathway	activated
Viral myokarditis	activated
Natural killer cell mediated cytotoxicity	activated
T cell receptor signaling pathway	activated
Notch signaling pathway	activated
Pathways in cancer	activated
JAK-STAT singaling pathway	activated
Tight junction	activated
Retrograde endocannabinoid signaling	activated
Cholinergic synapse	activated
Dopaminergic synapse	activated
Adipocytokine signaling pathway	activated
B cell receptor signaling pathway	activated
Regulation of actin cytoskeleton	activated
Focal adhesion	activated
ARVC	inhibited
ECM-receptor interaction	inhibited
MAPK signaling pathway	inhibited
Gap junction	inhibited
Glutamatergic synapse	inhibited
Phosphatidylinositol signaling systém	inhibited

Conclusion

Differences in gene expression in the aneurysmal tissue and in the biopsy of healthy tissue of the same patient were found. The changes detected were related to the inflammatory process regulation by means of immune mechanisms - inflammation mediated by chemokine and cytokine signaling pathways, integrin signaling pathway, T and B cell activation. Besides, changes in the expression of genes involved in intercellular and intracellular signaling systems were identified. Knowledge of these mechanisms can help get better understanding of the pathogenesis and treatment of AAAs.

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