·基础研究·

桃红四物汤对兔自体皮片移植模型 Delta-like 4 表达的影响

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摘　要　目的:观察桃红四物汤对兔自体皮片移植模型 Delta-like 4 表达的影响。**方法:**将 75 只新西兰大白兔(10～12 月龄)随机分为假手术组、模型组、低剂量组、中剂量组和高剂量组,每组 15 只。模型组、低剂量组、中剂量组和高剂量组动物进行自体皮片移植手术,假手术组仅在对应区域作切口,不进行皮下组织分离。造模术后假手术组和模型组动物以蒸馏水灌胃,低剂量组、中剂量组和高剂量组均以制备好的桃红四物汤汤剂灌胃(每次给药量分别为 2.5 g·kg^{-1}、5 g·kg^{-1}、10 g·kg^{-1}),每天 2 次。分别在药物干预开始后 2、5、8 d 从每组随机选取 5 只动物,心脏采血后处死,切取移植皮片吻合区皮片组织。采用酶联免疫吸附实验测定血清 Delta-like 4 蛋白含量;所取皮片组织分成 2 份,一份制成石蜡切片,HE 染色后测定血管密度,另一份采用逆转录聚合酶链式反应法测定 Delta-like 4 mRNA 含量。**结果:**①血清 Delta-like 4 蛋白含量。药物干预开始后 2 d,5 组动物血清 Delta-like 4 蛋白含量比较,差异无统计学意义[(30.58 ± 3.56) ng·mL^{-1},(32.31 ± 2.66) ng·mL^{-1},(33.53 ± 1.75) ng·mL^{-1},(36.00 ± 1.49) ng·mL^{-1},(35.63 ± 1.87) ng·mL^{-1},F = 2.669,P = 0.062]。药物干预开始后 5、8 d,5 组动物血清 Delta-like 4 蛋白含量比较,组间差异均有统计学意义[(30.56 ± 1.35) ng·mL^{-1},(33.52 ± 2.50) ng·mL^{-1},(37.96 ± 1.83) ng·mL^{-1},(48.74 ± 2.34) ng·mL^{-1},(49.05 ± 2.86) ng·mL^{-1},F = 46.239,P = 0.000;(29.26 ± 2.20) ng·mL^{-1},(32.98 ± 1.43) ng·mL^{-1},(35.24 ± 1.97) ng·mL^{-1},(38.02 ± 1.72) ng·mL^{-1},(36.06 ± 2.50) ng·mL^{-1},F = 8.394,P = 0.000];模型组分别与假手术组和低剂量组比较,差异均无统计学意义(5 d:P = 0.112,P = 0.269;8 d:P = 0.340,P = 0.182);中、高剂量组血清 Delta-like 4 蛋白含量均高于模型组(5 d:P = 0.000,P = 0.000;8 d:P = 0.020,P = 0.006);中、高剂量组比较,组间差异均无统计学意义(P = 0.862,P = 0.245)。药物干预后 5 d,中、高剂量组血清 Delta-like 4 蛋白含量均高于低剂量组(P = 0.000,P = 0.000)。药物干预开始后 8 d,中、高剂量组 Delta-like 4 蛋白含量与低剂量组比较,差异均无统计学意义(P = 0.105,P = 0.623)。②移植皮片组织中 Delta-like 4 mRNA 含量。药物干预开始后 2、5、8 d,5 组动物移植皮片中 Delta-like 4 mRNA 含量比较,组间差异均有统计学意义(0.26 ± 0.03,0.29 ± 0.04,0.34 ± 0.06,0.42 ± 0.03,0.39 ± 0.04,F = 7.072,P = 0.001;0.25 ± 0.03,0.34 ± 0.04,0.39 ± 0.03,0.48 ± 0.06,0.45 ± 0.06,F = 12.028,P = 0.001;0.25 ± 0.06,0.30 ± 0.04,0.35 ± 0.03,0.44 ± 0.03,0.43 ± 0.04,F = 10.813,P = 0.000);模型组分别与假手术组和低剂量组比较,差异均无统计学意义(2 d:P = 0.452,P = 0.162;5 d:P = 0.320,P = 0.158;8 d:P = 0.171,P = 0.219);模型组 Delta-like 4 mRNA 含量低于中、高剂量组(2 d:P = 0.000,P = 0.001;5 d:P = 0.001,P = 0.009;8 d:P = 0.001,P = 0.002);中、高剂量组比较,组间差异均无统计学意义(P = 0.426,P = 0.330,P = 0.725)。药物干预开始后 2 d,中、高剂量组与低剂量组比较,差异均无统计学意义(P = 0.111,P = 0.167);药物干预开始后 5、8 d,中、高剂量组 Delta-like 4 mRNA 含量均高于低剂量组(5 d:P = 0.024,P = 0.025;8 d:P = 0.013,P = 0.028)。③移植皮片组织中血管密度。药物干预开始后 2、5 d,5 组动物移植皮片中每个视野(×400)中血管数量比较,组间差异均有统计学意义[(5.37 ± 0.36)个,(2.55 ± 0.41)个,(2.83 ± 0.24)个,(3.31 ± 0.26)个,(3.53 ± 0.67)个,F = 4.084,P = 0.014;(5.62 ± 0.56)个,(4.25 ± 0.68)个,(4.80 ± 0.74)个,(5.88 ± 0.42)个,(5.92 ± 0.48)个,F = 4.600,P = 0.009];模型组均低于假手术组(P = 0.001,P = 0.011),模型组与低剂量组比较,差异均无统计学意义(P = 0.527,P = 0.268);中、高剂量组比较,组间差异均无统计学意义(P = 0.620,P = 0.939)。药物干预开始后 2 d,中、高剂量组与模型组比较,差异均无统计学意义(P = 0.102,P = 0.131);中、高剂量组与低剂量组比较,差异均无统计学意义(P = 0.297,P = 0.352)。药物干预开始后 5 d,中、高剂量组高于模型组(P = 0.003,P = 0.003);中、高剂量组与低剂量组比较,差异均无统计学意义(P = 0.038,P = 0.033)。药物干预开始后 8 d,5 组动物移植皮片中每个视野中血管数量比较,差异无统计学意义[(6.18 ± 0.33)个,(5.86 ± 0.66)个,(6.03 ± 0.40)个,(6.27 ± 0.53)个,(6.27 ± 0.59)个,F = 0.334,P = 0.852]。**结论:**桃红四物汤能上调兔自体皮片移植模型 Delta-like 4 的表达,促进血管新生。但本研究未能明确桃红四物汤的剂量及作用时间与其上调 Delta-like 4 表达作用的关系,需要在今后的研究中进一步探讨。

关键词　桃红四物汤;皮肤移植;Notch 信号通路;兔;动物实验

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Impact of Taohong Siwu Tang(桃红四物汤) on Delta-like 4 expression in the autologous skin graft model of rabbits

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ABSTRACT **Objective**:To observe the impact of Taohong Siwu Tang(桃红四物汤,THSWT) on Delta-like 4 expression in the autologous skin graft model of rabbits. **Methods**:Seventy-five New Zealand rabbits which ranged in age from 10 to 12 months were randomly divided into sham-operated group,model group,low-dose group,middle-dose group and high-dose group,15 cases in each group. The autologous skin transplantation surgery were performed on rabbits in model group,low-dose group,middle-dose group and high-dose group,while sham operation were performed on rabbits in sham-operated group. After the modeling operation,the rabbits in sham-operated group and model group were intragastric administrated with distilled water;while the others in low-dose group,middle-dose group and high-dose group were intragastric administrated with the prepared THSWT in dosages of 2.5,5 and 10 g/kg at a time,twice a day. Five rabbits were randomly selected from each group and the blood samples were obtained from the heart at 2,5 and 8 days after the beginning of the drug intervention respectively. The rabbits were executed and their anastomotic skin graft tissues were fetched out. The serum content of Delta-like 4 protein were measured by using enzyme-linked immunosorbent assay(ELISA). The acquired skin tissues were divided into 2 parts,and one of them were maded into paraffin sections and the blood vessel density were measured after HE staining,while the other portion were applied to measure the Delta-like 4 mRNA level by using reverse transcription-polymerase chain reaction(RT-PCR). **Results**:There was no statistical difference in serum content of Delta-like 4 protein between the 5 groups at 2 days after the beginning of the drug intervention(30.58 +/− 3.56,32.31 +/− 2.66,33.53 +/− 1.75,36.00 +/− 1.49,35.63 +/− 1.87 ng/ml,$F=2.669$,$P=0.062$). There was statistical difference in serum content of Delta-like 4 protein between the 5 groups at 5 and 8 days after the beginning of the drug intervention(30.56 +/− 1.35,33.52 +/− 2.50,37.96 +/− 1.83,48.74 +/− 2.34,49.05 +/− 2.86 ng/ml,$F=46.239$,$P=0.000$;29.26 +/− 2.20,32.98 +/− 1.43,35.24 +/− 1.97,38.02 +/− 1.72,36.06 +/− 2.50 ng/ml,$F=8.394$,$P=0.000$). There was no statistical difference in serum content of Delta-like 4 protein between model group and sham-operated group and between model group and low-dose group(5d:$P=0.112$,$P=0.269$;8d:$P=0.340$,$P=0.182$). The serum content of Delta-like 4 protein were higher in middle-dose group and high-dose group compared to model group(5d:$P=0.000$,$P=0.000$;8d:$P=0.020$,$P=0.006$). There was no statistical difference in serum content of Delta-like 4 protein between middle-dose group and high-dose group($P=0.862$,$P=0.245$). The serum content of Delta-like 4 protein were higher in middle-dose group and high-dose group compared to low-dose group at 5 days after the beginning of the drug intervention($P=0.000$,$P=0.000$). There was no statistical difference in serum content of Delta-like 4 protein between middle-dose group and low-dose group and between high-dose group and low-dose group at 8 days after the beginning of the drug intervention($P=0.105$,$P=0.623$). There was statistical difference in mRNA level of Delta-like 4 in skin graft between the 5 groups at 2,5 and 8 days after the beginning of the drug intervention(0.26 +/− 0.03,0.29 +/− 0.04,0.34 +/− 0.06,0.42 +/− 0.03,0.39 +/− 0.04,$F=7.072$,$P=0.001$;0.25 +/− 0.03,0.34 +/− 0.04,0.39 +/− 0.03,0.48 +/− 0.06,0.45 +/− 0.06,$F=12.028$,$P=0.001$;0.25 +/− 0.06,0.30 +/− 0.04,0.35 +/− 0.03,0.44 +/− 0.03,0.43 +/− 0.04,$F=10.813$,$P=0.000$). There was no statistical difference in Delta-like 4 mRNA level between model group and sham-operated group and between model group and low-dose group(2 d:$P=0.452$,$P=0.162$;5 d:$P=0.320$,$P=0.158$;8 d:$P=0.171$,$P=0.219$). The Delta-like 4 mRNA level were lower in model group compared to middle-dose group and high-dose group(2 d:$P=0.000$,$P=0.001$;5 d:$P=0.001$,$P=0.009$;8 d:$P=0.001$,$P=0.002$). There was no statistical difference in Delta-like 4 mRNA level between middle-dose group and high-dose group($P=0.426$,$P=0.330$,$P=0.725$). There was no statistical difference in Delta-like 4 mRNA level between middle-dose group and low-dose group and between high-dose group and low-dose group at 2 days after the beginning of the drug intervention($P=0.111$,$P=0.167$). The Delta-like 4 mRNA level was higher in middle-dose group and high-dose group compared to low-dose group at 5 and 8 days after the beginning of the drug intervention(5 d:$P=0.024$,$P=0.025$;8 d:$P=0.013$,$P=0.028$). There was statistical difference in the number of blood vessels in skin graft under the optical microscope(×400) between the 5 groups at 2 and 5 days after the beginning of the drug intervention(5.37 +/− 0.36,2.55 +/− 0.41,2.83 +/− 0.24,3.31 +/− 0.26,3.53 +/− 0.67,$F=4.084$,$P=0.014$;5.62 +/− 0.56,4.25 +/− 0.68,4.80 +/− 0.74,5.88 +/− 0.42,5.92 +/− 0.48,$F=4.600$,$P=0.009$). The number of blood vessels was less in model group compared to sham-operated group($P=0.001$,$P=0.011$),and there was no statistical difference in the number of blood vessels between model group and low-dose group($P=0.527$,$P=0.268$) and between middle-

dose group and high-dose group($P=0.620$,$P=0.939$). At 2 days after the beginning of the drug intervention, there was no statistical difference in the number of blood vessels between middle-dose group and model group($P=0.102$) and between high-dose group and model group($P=0.131$) and between middle-dose group and low-dose group($P=0.297$) and between high-dose group and low-dose group($P=0.352$). At 5 days after the beginning of the drug intervention, the number of blood vessels was more in middle-dose group and high-dose group compared to model group($P=0.003$,$P=0.003$), while no statistical difference was found between middle-dose group and low-dose group and between high-dose group and low-dose group($P=0.038$,$P=0.033$). At 8 days after the beginning of the drug intervention, there was no statistical difference in the number of blood vessels in skin graft under the optical microscope(×400) between the 5 groups (6.18 +/− 0.33,5.86 +/− 0.66,6.03 +/− 0.40,6.27 +/− 0.53,6.27 +/− 0.59,$F=0.334$,$P=0.852$). **Conclusion**: THSWT can up-regulate Delta-like 4 expression and promote angiogenesis in autologous skin graft model of rabbits. However, we cann't clarify the relationship between the role of THSWT in up-regulating Delta-like 4 expression and its dose and action time, which need to be further studied.

Key words Taohong Siwu Tang; skin transplantation; Notch Signaling Pathway; rabbits; animal experimentation

自体皮片移植术是目前治疗皮肤缺损最常用、最有效的方法,皮片移植术后皮片形成的新血管网的质量决定了皮片能否存活。Notch 信号通路配体 Delta-like 4 参与血管新生的全过程,调控血管形成[1-6]。我们前期的研究证实,桃红四物汤能有效促进皮片移植术后皮片的生长[7]。本研究拟通过实验观察桃红四物汤对兔自体皮片移植模型 Delta-like 4 表达的影响。

1 材料与仪器

1.1 实验动物 健康清洁级新西兰大白兔 75 只,10~12月龄,雌雄各半,体质量 2.0~2.5 kg,由湖南中医药大学动物实验中心代购,实验动物许可证号:SCXK(湘)2009-0012。实验方案通过医学实验动物伦理委员会批准。

1.2 实验药物和试剂 桃红四物汤,药物组成包括生地 20 g、当归 20 g、赤芍 g、川芎 10 g、桃仁 20 g、红花 10 g[7]。煎煮后浓缩,制成含生药 4 g·mL^{-1}的汤剂冷藏保存。eBioscience 酶联免疫吸附实验(enzyme-linked immuno sorbent assay, ELISA)试剂盒(上海晶天生物科技有限公司)。聚合酶链式反应(polymerase chain reaction, PCR)引物由上海生工生物工程有限公司合成,上游引物 CTG CCT ATC TGC CTT TCT G;下游引物 ACA GCC ATT GTG AGG GAT G。

1.3 实验仪器 DNP-9162 型电热恒温培养箱(上海精宏实验设备有限公司);Promega A6001-GoTaq® qPCR Master Mix(上海叶舟生物科技有限公司);820 型 AO 切片机(Reichert 公司);BX50 型光学显微镜(OLYMPUS 公司)。

2 方 法

2.1 分组及造模 适应性喂养 1 周后按体质量排序、标号,采用随机数字表将 75 只动物随机分为假手术组、模型组、低剂量组、中剂量组和高剂量组,每组 15 只。造模手术前 6 h 禁食、禁水,以 20 mg·kg^{-1}耳缘静脉注射 3% 戊巴比妥钠进行麻醉。将模型组、低剂量组、中剂量组和高剂量组动物固定在兔台上,先在其背部自 T_3 棘突右侧 1 cm 处向尾部切取 6 cm×3 cm×0.05 cm 的长方形皮片,再从腹部切取相同规格的皮片,修整后移植于背部皮肤缺损区,间断缝合,加压包扎,腹部切口直接拉拢缝合。假手术组仅在背部和腹部相应区域用作相同规格的切口,深达皮下组织,但不进行皮下组织分离,间断缝合切口。

2.2 药物干预 造模术后假手术组和模型组动物以蒸馏水灌胃,每次 10 mL,每天 2 次;低剂量组、中剂量组和高剂量组均以制备好的桃红四物汤汤剂灌胃,每次给药量分别为 2.5 g·kg^{-1}、5 g·kg^{-1}、10 g·kg^{-1},每天 2 次。

2.3 血清 Delta-like 4 蛋白含量、移植皮片组织中 Delta-like 4 mRNA 含量及血管密度测定 分别在药物干预开始后 2、5、8 d 从每组随机选取 5 只动物,心脏采血后处死,切取移植皮片吻合区皮片组织。将所采集的血液离心后取血清,按照 eBioscience ELISA 试剂盒上的操作步骤,测定 Delta-like 4 蛋白含量。将所取皮片组织分成 2 份,其中一份制成石蜡切片,HE 染色后在光镜下计算血管密度,以每个视野下毛细管横断面的数量来表示;另一份采用逆转录 PCR 法测定 Delta-like 4 mRNA 含量。

2.4 数据统计分析 采用 SPSS 17.0 软件对所得数据进行统计学分析,5 组动物同一时点血清 Delta-like 4 蛋白含量、移植皮片中 Delta-like 4 mRNA 含量及血管密度的组间比较采用方差分析,组间两两比较采用

LSD－t检验,检验水准$\alpha=0.05$。

3　结　果

3.1　血清Delta-like 4蛋白含量　药物干预开始后2 d,5组动物血清Delta-like 4蛋白含量比较,差异无统计学意义。药物干预开始后5、8 d,5组动物血清Delta-like 4蛋白含量比较,组间差异均有统计学意义;模型组分别与假手术组和低剂量组比较,差异均无统计学意义(5 d:$P=0.112$,$P=0.269$;8 d:$P=0.340$,$P=0.182$);中、高剂量组血清Delta-like 4蛋白含量均高于模型组(5 d:$P=0.000$,$P=0.000$;8 d:$P=0.020$,$P=0.006$);中、高剂量组比较,组间差异均无统计学意义($P=0.862$,$P=0.245$)。药物干预后5 d,中、高剂量组血清Delta-like 4蛋白含量均高于低剂量组($P=0.000$,$P=0.000$)。药物干预开始后8 d,中、高剂量组蛋白含量与低剂量组比较,差异均无统计学意义($P=0.105$,$P=0.623$)。见表1。

表1　药物干预开始后不同时点5组动物血清Delta-like 4蛋白含量　$\bar{x}\pm s$,ng·mL^{-1}

组别	样本量(只)	药物干预开始后时间点		
		2 d	5 d	8 d
假手术组	5	30.58±3.56	30.56±1.35	29.26±2.20
模型组	5	32.31±2.66	33.52±2.50	32.98±1.43
低剂量组	5	33.53±1.75	37.96±1.83	35.24±1.97
中剂量组	5	36.00±1.49	48.74±2.34	38.02±1.72
高剂量组	5	35.63±1.87	49.05±2.86	36.06±2.50
F值		2.669	46.239	8.394
P值		0.062	0.000	0.000

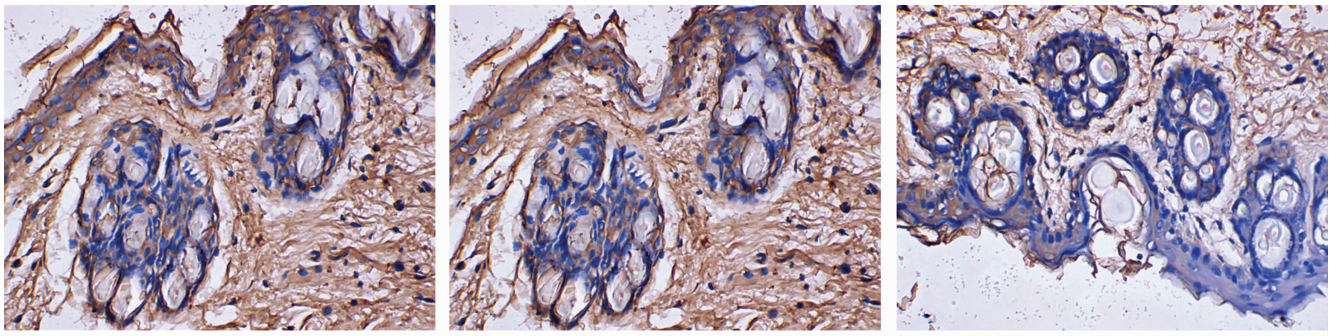
3.2　移植皮片组织中Delta-like 4 mRNA含量　药物干预开始后2、5、8 d,5组动物移植皮片中Delta-like 4 mRNA含量比较,组间差异均有统计学意义;模型组分别与假手术组和低剂量组比较,差异均无统计学意义(2 d:$P=0.452$,$P=0.162$;5 d:$P=0.320$,$P=0.158$;8 d:$P=0.171$,$P=0.219$);模型组Delta-like 4 mRNA含量低于中、高剂量组(2 d:$P=0.000$,$P=0.001$;5 d:$P=0.001$,$P=0.009$;8 d:$P=0.001$,$P=0.002$);中、高剂量组比较,组间差异均无统计学意义($P=0.426$,$P=0.330$,$P=0.725$)。药物干预开始后2 d,中、高剂量组与低剂量组比较,差异均无统计学意义($P=0.111$,$P=0.167$);药物干预开始后5、8 d,中、高剂量组Delta-like 4 mRNA含量均高于低剂量组(5 d:$P=0.024$,$P=0.025$;8 d:$P=0.013$,$P=0.028$)。见表2。

表2　药物干预开始后不同时点5组动物移植皮片中Delta-like 4 mRNA含量　$\bar{x}\pm s$

组别	样本量(只)	药物干预开始后时间点		
		2 d	5 d	8 d
假手术组	5	0.26±0.03	0.25±0.03	0.25±0.06
模型组	5	0.29±0.04	0.34±0.04	0.30±0.04
低剂量组	5	0.34±0.06	0.39±0.03	0.35±0.03
中剂量组	5	0.42±0.03	0.48±0.06	0.44±0.03
高剂量组	5	0.39±0.04	0.45±0.06	0.43±0.04
F值		7.072	12.028	10.813
P值		0.001	0.001	0.000

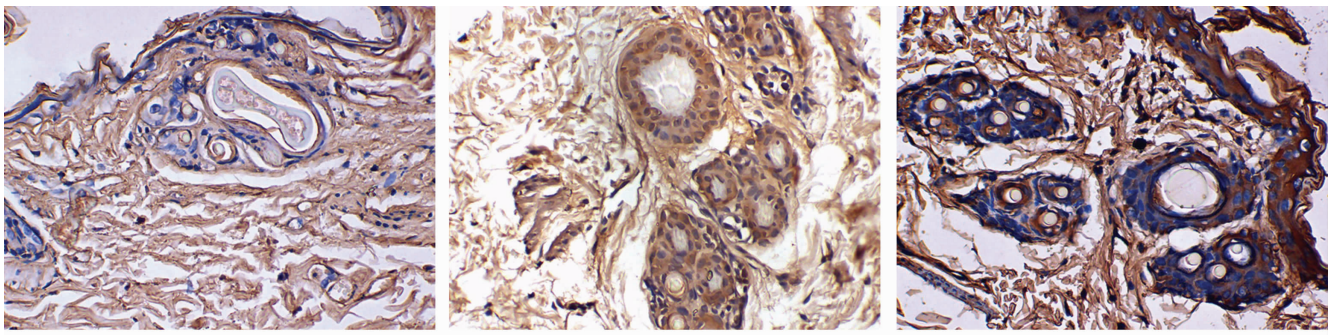
3.3　移植皮片组织中血管密度　药物干预开始后2、5 d,5组动物移植皮片中每个视野(×400)中血管数量比较,组间差异均有统计学意义;模型组均低于假手术组($P=0.001$,$P=0.011$),模型组与低剂量组比较,差异均无统计学意义($P=0.527$,$P=0.268$);中、高剂量组比较,组间差异均无统计学意义($P=0.620$,$P=0.939$)。药物干预开始后2 d,中、高剂量组与模型组比较,差异均无统计学意义($P=0.102$,$P=0.131$);中、高剂量组与低剂量组比较,差异均无统计学意义($P=0.297$,$P=0.352$)。药物干预开始后

5 d,中、高剂量组血管密度均高于模型组（$P=0.003$，$P=0.003$）；中、高剂量组与低剂量组比较，差异均无统计学意义（$P=0.038$，$P=0.033$）。药物干预开始后 8 d,5 组动物移植皮片中每个视野中血管数量比较，差异无统计学意义。见图 1 至图 5 及表 3。



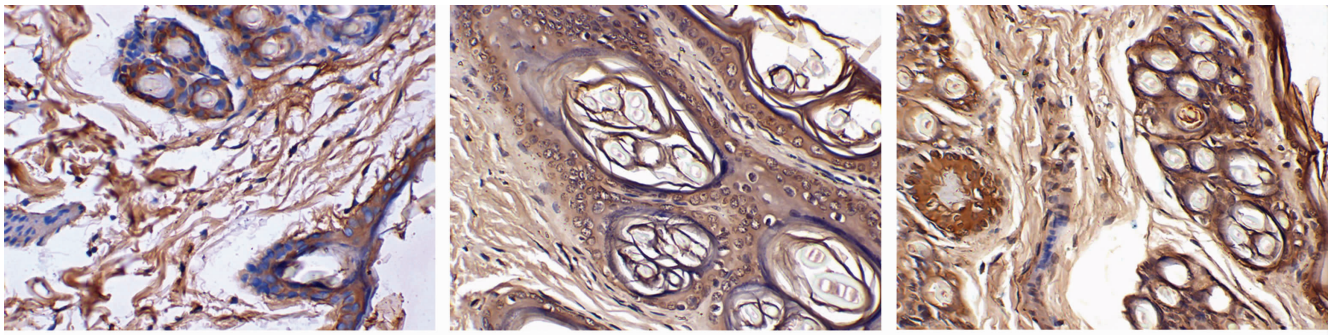
(1) 药物干预开始后2 d　(2) 药物干预开始后5 d　(3) 药物干预开始后8 d

图 1　假手术组移植皮片组织切片（HE 染色　×400）



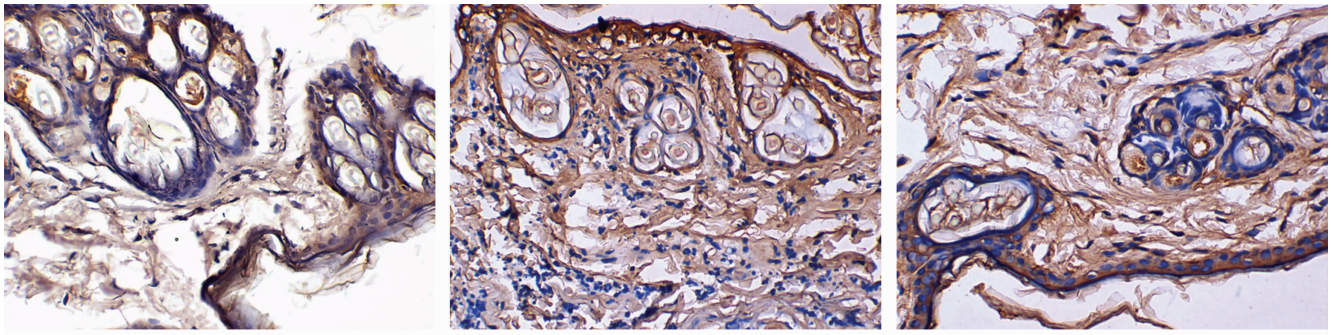
(1) 药物干预开始后2 d　(2) 药物干预开始后5 d　(3) 药物干预开始后8 d

图 2　模型组移植皮片组织切片（HE 染色　×400）



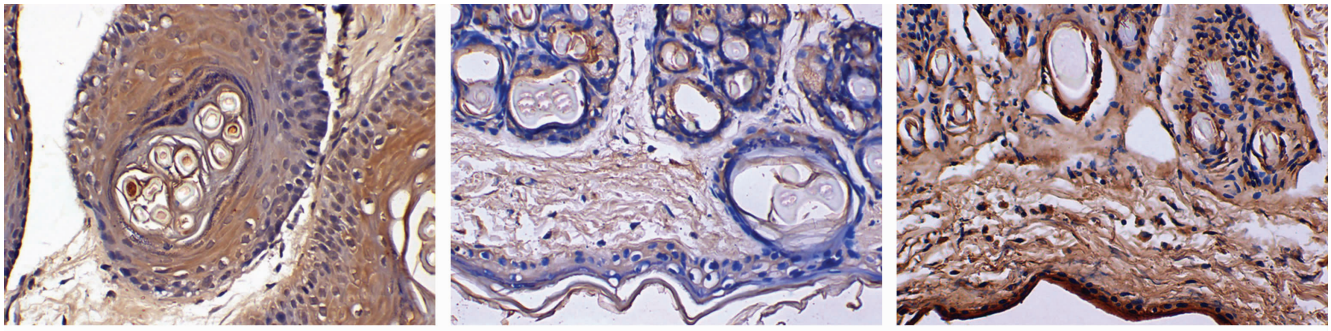
(1) 药物干预开始后2 d　(2) 药物干预开始后5 d　(3) 药物干预开始后8 d

图 3　低剂量组移植皮片组织切片（HE 染色　×400）



(1) 药物干预开始后2 d　(2) 药物干预开始后5 d　(3) 药物干预开始后8 d

图 4　中剂量组移植皮片组织切片（HE 染色　×400）



(1) 药物干预开始后2 d　(2) 药物干预开始后5 d　(3) 药物干预开始后8 d

图 5　高剂量组移植皮片组织切片（HE 染色　×400）

表 3　药物干预开始后不同时点 5 组动物移植皮片每个视野（×400）中血管数量　$\bar{x} \pm s$，个

组别	样本量（只）	药物干预开始后时间点		
		2 d	5 d	8 d
假手术组	5	5.37 ± 0.36	5.62 ± 0.56	6.18 ± 0.33
模型组	5	2.55 ± 0.41	4.25 ± 0.68	5.86 ± 0.66
低剂量组	5	2.83 ± 0.24	4.80 ± 0.74	6.03 ± 0.40
中剂量组	5	3.31 ± 0.26	5.88 ± 0.42	6.27 ± 0.53
高剂量组	5	3.53 ± 0.67	5.92 ± 0.48	6.27 ± 0.59
F 值		4.084	4.600	0.334
P 值		0.014	0.009	0.852

4　讨　论

当机体组织遭到破坏后，Notch 信号通路激活，Delta-like 4 与受体结合后，进入细胞核发挥生物学作用[8]，并与表皮生长因子形成负反馈[9-10]，影响内皮细胞生长[11-12]。该通路通过增加血管出芽，增加血管数量，减少血管畸形，参与相应的修复过程[13-14]。机体受到创伤 48 h 后，部分经历完炎症反应期，开始进入细胞增殖期。随着皮片与创面之间毛细血管网的逐渐建立，皮片进入血管营养期，1 周后新生的血管构建成熟血管系统。最后进入组织修复期，完善机体功能。

本实验中，药物干预后，桃红四物汤中、高剂量组 Delta-like 4 表达量和皮片中血管密度较高，高于低剂量组和模型组，中、高剂量组之间比较，差异无统计学意义。提示中、高剂量的桃红四物汤可上调 Delta-like 4 表达，促进血管新生。现代药理研究表明，桃红四物汤能促进局部血液循环，扩张血管[15]，其含药血清能保护内皮细胞，促进细胞增殖，增加细胞活力[16]。董大力等[17]的研究表明，桃红四物汤能明显促进大鼠随意皮瓣移植术后皮肤吻合区的血管再生能力，提高皮瓣存活率。石毅等[18-19]的研究表明，Notch 信号通路参与血管机械力信号的调控，而且血流量的改变能够调节 Delta-like 4 的表达。

本研究的结果提示，桃红四物汤能上调兔自体皮片移植模型 Delta-like 4 的表达，促进血管新生。但本研究未能明确桃红四物汤的剂量及作用时间与其上调 Delta-like 4 表达作用的关系，需要在今后的研究中进一步探讨。

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