

激活豚鼠耳蜗螺旋动脉平滑肌细胞连接蛋白43下调 衰老蛋白P16和P21的表达*

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【摘要】目的 通过D-半乳糖(D-galactose, D-gal)干预制备豚鼠耳蜗螺旋动脉(SMA)平滑肌细胞衰老模型,分析连接蛋白43(Cx43)与衰老相关蛋白P16和P21表达的相关性,探讨Cx43在细胞衰老中可能发挥的作用。**方法** 用贴壁法培养豚鼠SMA平滑肌细胞,应用免疫荧光技术检测平滑肌细胞标记物。实验分对照组、D-gal组和D-gal+缝隙连接激动剂AAP10干预组(AAP10组)。CCK-8检测各组平滑肌细胞活性,确定D-gal干预浓度及时间;qRT-PCR检测各组Cx43 mRNA表达;Western blot检测各组Cx43、P16和P21的蛋白表达量;免疫荧光技术检测各组P16、P21的表达分布情况。**结果** 免疫荧光检测结果显示细胞肌动蛋白(α -SM-actin)阳性表达率达90%以上;CCK-8检测结果显示D-gal最佳干预浓度为30 mg/mL,干预时间为48 h;qRT-PCR检测发现D-gal组平滑肌细胞上Cx43 mRNA水平较对照组降低($P<0.01$);AAP10组较D-gal组细胞Cx43 mRNA水平上调($P<0.01$);Western blot检测发现D-gal组平滑肌细胞上Cx43蛋白水平较对照组降低($P<0.01$);P16和P21蛋白表达较对照组升高($P<0.01$);AAP10组较D-gal组细胞Cx43蛋白表达上调($P<0.01$),P16、P21蛋白表达下调($P<0.01$);免疫荧光结果显示P16和P21主要表达于细胞核上,P16和P21蛋白在D-gal组较对照组细胞荧光强度升高,AAP10组较D-gal组荧光强度下降($P<0.01$)。**结论** 上调Cx43的表达可以逆转D-gal诱导的SMA上衰老相关蛋白P16和P21的表达异常。提示Cx43可能参与细胞衰老过程,为延缓细胞衰老提供理论依据和可能的干预靶点。

【关键词】 细胞衰老 耳蜗螺旋动脉 Cx43 D-半乳糖

Down-regulation of the Expression of Senescence Proteins P16 and P21 by Activating Connexin 43 in the Smooth Muscle of Spiral Modiolar Artery of Guinea Pigs HU Na¹, SI Chao², ZHANG Zhi-ping³, MA Ke-tao⁴, ZHANG Liang^{4△}.

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【Abstract】 Objective To analyze the correlation between connexin 43 (Cx43) and the expression of P16 and P21, aging-related proteins, and to investigate the possible role of Cx43 in the development of cell senescence with an aging model prepared by D-galactose (D-gal) intervention in the vascular smooth muscle cells (VSMCs) of guinea pig spiral modiolar artery (SMA). **Methods** The VSMCs of guinea pig SMA were cultured with the adhesion method, and the markers of VSMCs were detected with immunofluorescence technique. The experiment has a control group, a D-gal group, and a group that received D-gal and gap junction agonist AAP10 intervention, hereafter referred to as the AAP10 group. Cell Counting Kit-8 (CCK-8) was used to check VSMC activity and to determine the concentration and duration of D-gal intervention. The mRNA expression of Cx43 in each group was checked with qRT-PCR. The expression of Cx43, P16 and P21 proteins in each group was examined with the Western blot. The expression and distribution of P16 and P21 proteins were examined with immunofluorescence assay. **Results** Immunofluorescence results showed that the positive expression rate of cell actin (α -SM-actin) was over 90%. CCK-8 results showed that the optimal concentration of D-gal intervention was 30 mg/mL and the intervention duration was 48 h. qRT-PCR test showed that the mRNA expression of Cx43 in VSMCs in the D-gal group was significantly lower than that in the control group ($P<0.01$), while it is higher in the AAP10 group than that of the D-gal group ($P<0.01$); Western blot assay showed that the Cx43 expression level in VSMCs in the D-gal group was significantly lower than that in the control group ($P<0.01$) and the expression of P16 and P21 was

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significantly higher than that in the control group ($P < 0.01$), the expression of Cx43 protein in AAP10 group was significantly up-regulated compared with that in the D-gal group ($P < 0.01$), while the expression of P16 and P21 was down-regulated significantly ($P < 0.01$); The results of immunofluorescence showed that P16 and P21 were mainly expressed in the cell nucleus. Semi-quantitative analysis of fluorescence intensity showed that the level of P16 and P21 protein in the D-gal group was significantly higher than that in the control group, and the fluorescence intensity of AAP10 group was significantly lower than that in the D-gal group ($P < 0.01$). **Conclusion** Up-regulation of Cx43 expression can reverse the D-gal-induced abnormal expression of P16 and P21, two aging-related proteins, in SMA. It is suggested that Cx43 on SMA may be involved in D-gal-induced cell senescence, which provides a theoretical basis and possible intervention target for the delay of cell senescence.

【Key words】 Cell senescence Cochlear spiral artery Cx43 D-galactose

机体衰老时的变化是多方面的,如细胞内部结构与功能的变化以及各种组织器官出现功能障碍。听力损伤是影响全球老年人最普遍的病症之一^[1]。耳蜗螺旋动脉(SMA)是唯一参与和供应耳蜗循环系统的动脉,它由内皮细胞以及血管平滑肌细胞(VSMCs)组成,细胞间具有多种连接方式,其中以缝隙连接方式最为多见,连接蛋白(connexin, Cx)则是缝隙连接与半通道的基本单位^[2],其中Cx43在VSMCs中表达量位居第一^[3],说明Cx43对血管的功能扮演着十分重要的角色。作为一种常见的缝隙连接激动剂^[4],抗心律失常肽(即缝隙连接激动剂AAP10)可上调Cx43的表达。有文献报道,噪声能够引起耳蜗外侧壁螺旋韧带受损,使螺旋韧带上Cx26及Cx31表达降低^[5]。然而有关Cx43与耳蜗螺旋动脉VSMCs衰老关系报道较少。因此,本实验通过建立D-半乳糖(D-galactose, D-gal)致原代豚鼠耳蜗螺旋动脉VSMCs衰老模型,观察Cx43的表达变化以及给予AAP10干预后衰老指标P16、P21的变化,从而初步探讨Cx43在延缓耳蜗螺旋动脉VSMCs衰老中可能发挥的作用。

1 材料和方法

1.1 主要试剂和仪器

DMEM/F-12培养基、青霉素-链霉素双抗(美国Gibco公司);小鼠单克隆抗体 β -actin、Anti-Cx43、Anti-P16、Anti-P21(美国Abcam公司);D-gal、 α -SAM-actin抗体、碘化丙啶(PI,美国Sigma公司);LSM510激光共聚焦显微镜(德国CarlZeiss公司);抗心律失常肽AAP10(中国杭州中肽公司);FITC山羊抗鼠IgG二抗、FITC山羊抗兔IgG二抗(中国中杉金桥生物公司);逆转录试剂盒(美国Thermo公司)。

1.2 原代耳蜗螺旋动脉VSMCs培养

购买清洁级雄性和雌性豚鼠(新疆医科大学动物实验中心),购买后在洁净条件下共同饲养,自然交配后分娩新生乳鼠。取豚鼠新生乳鼠3只,麻醉,断头处死,在无菌环境下迅速分离提取SMA, PBS冲洗,将其于EP管中剪碎,每小块平均体积4 mm左右,均匀平铺于无菌培养皿

的底部,滴加少量含20%(体积分数)胎牛血清的DMEM/F-12完全培养基,倒扣置于37℃、体积分数5%CO₂培养箱中进行培养,2 h后翻转培养皿,小心滴加,3 mL含20%(体积分数)胎牛血清的DMEM/F-12培养基,静置3 d,随后每3 d更换一次培养基,一周后在显微镜下可见每一组织小块边缘有大片细胞爬出,细胞为梭形,取原代细胞进行爬片、干预,按照说明书步骤对细胞进行固定、透化以及封闭处理后加入 α -SM-actin一抗在4℃条件下过夜孵育。第二天加入相应的荧光二抗以及滴加少量DAPI溶液染核、封片,应用共聚焦显微镜进行成像。继续培养待培养皿底部的细胞密度长至90%左右,将其传代和冻存以备后用。

1.3 CCK-8法检测各组细胞活性

在96孔板中接种浓度为 1×10^4 mL⁻¹的细胞悬液(100 μ L/孔)。将培养板放在培养箱中预培养(37℃,体积分数5%CO₂)。0、7.5、15、30、60 mg/mL D-gal分别作用于原代VSMCs 0、12、24、48、72 h,每孔加入10 μ L CCK-8溶液,将培养板在培养箱内孵育2 h。用酶标仪测定在450 nm处的吸光度。细胞活性(%)=(治疗组吸光度值-空白组吸光度值)/(对照组吸光度值-空白组吸光度值) $\times 100\%$ 。

1.4 免疫荧光技术观察P16和P21的表达和分布情况

取代数靠前并且状态良好的细胞进行爬片,干预,按照说明书步骤依次对细胞进行固定、透化以及封闭处理后,分别加入P16一抗和P21一抗在4℃条件下过夜孵育。第二天每组各加入相应的荧光二抗以及滴加少量DAPI溶液染核,封片,应用共聚焦显微镜进行采像。

1.5 制备细胞衰老模型及分组

取代数靠前并且细胞状态良好的原代VSMCs进行分组干预。对照组:在37℃、体积分数5%CO₂培养箱中用含20%(体积分数)胎牛血清的DMEM/F-12完全培养基对细胞进行正常培养;D-gal组:加入30 mg/mL的D-gal于培养箱中培养48 h,制备细胞衰老模型;AAP10组:在含

20%(体积分数)胎牛血清的DMEM/F-12完全培养基内先加入浓度为100 nmol/L的AAP10,培养1 h后再加入30 mg/mL D-gal继续培养48 h;收集各组细胞置于-80 °C冰箱备用。

1.6 qRT-PCR检测各组VSMCs细胞Cx43 mRNA表达

采用RNeasy Mini Kit试剂盒提取各组细胞总RNA,先将其70 °C预变性5 min,42 °C退火60 min,最后4 °C延伸5 min,最终反转录为cDNA。 β -actin上游引物为5'-CGTAAAGACCTCTATGCCAACA-3',下游引物为5'-AGCCACCAATCCACACAGAG-3',扩增产物长度163 bp;Cx43上游引物为5'-GCTCCACTCTCGCTATGTC-3',下游引物为5'-TAGTTGCGCCAGTTTTGCTC-3',扩增产物长度113 bp。引物由上海生工有限公司合成。反应条件如下:首先95 °C预变性2 min,然后94 °C变性30 s,最后55 °C退火30 s,40次循环。采用 $2^{-\Delta\Delta Ct}$ 法处理各组实验数据进行统计学分析。

1.7 Western blot检测各组细胞Cx43蛋白的表达

将培养基中细胞密度调整为 $1 \times 10^6 \text{ mL}^{-1}$,按照分组给

与不同培养条件并收集各组豚鼠SMA,利用蛋白裂解液(PMSF:高效RIPA=1:100)提取蛋白,冻存备用。每孔上样30 μg 蛋白,将其进行恒压电泳、恒压转膜、奶粉封闭后,依次孵育内参 β -actin及Cx43的一抗和二抗。TBST洗膜后曝光,曝光后将胶片放入凝胶成像仪扫描采图,并采用Image J 2x软件分析各组条带灰度值,以目的条带与内参条带灰度比值代表目的蛋白的表达水平。

1.8 统计学方法

实验结果数据以 $\bar{x} \pm s$ 表示。多组间比较采用One-way ANOVA单因素方差分析,两样本均数 t 检验用于两组间的比较, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 原代耳蜗螺旋动脉VSMCs的鉴定

免疫荧光检查结果表明,在培养的原代细胞中,细胞呈“梭形”,且 α -SM-actin(VSMCs特异性表达的肌动蛋白)阳性表达数占细胞总数的90%以上(图1),说明原代培养耳蜗螺旋动脉VSMCs成功。

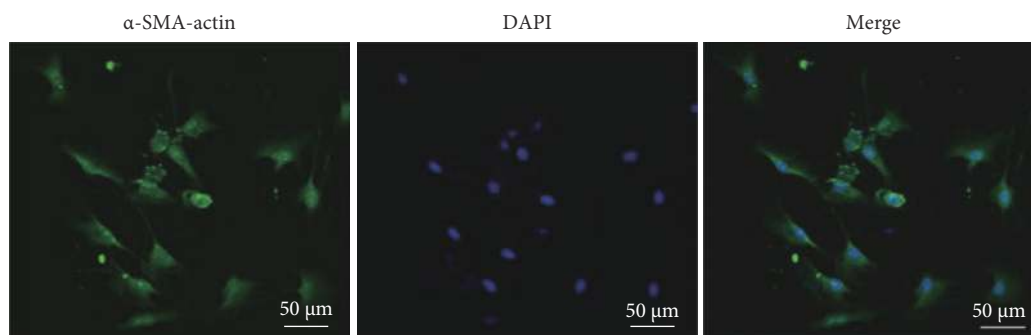


图1 原代VSMCs免疫荧光染色鉴定。 $\times 200$

Fig 1 Identification of primary VSMCs by immunofluorescence staining. $\times 200$

Expression of α -SMA-actin in VSMCs (green fluorescence); DAPI labeled nuclei (blue fluorescence).

2.2 CCK-8法检测各组VSMCs细胞活性

结果(图2)显示在0、7.5、15、30 mg/mL D-gal干预VSMCs 48 h以内时,不会严重影响细胞活性,细胞活性都在80%以上,干预时间大于48 h时就开始出现细胞活性的明显降低;当60 mg/mL D-gal作用于细胞12 h后就会开始严重影响细胞活性($P < 0.01$),因此选择30 mg/mL D-gal为制备VSMCs衰老模型的终浓度,干预时间为48 h。

2.3 各组VSMCs细胞Cx43 mRNA的表达

相比于对照组(1.00 ± 0.05)和AAP10组(0.81 ± 0.04),D-gal组(0.50 ± 0.03)Cx43 mRNA表达水平降低($P < 0.01$)。

2.4 各组VSMCs细胞上Cx43蛋白表达

由Western blot实验结果可以看出(图3),相比于对照

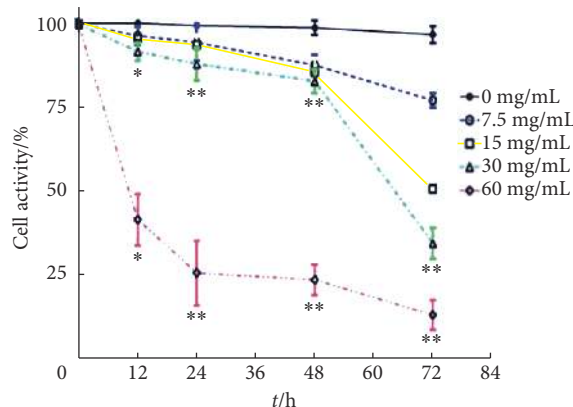


图2 D-gal对VSMCs细胞活性的影响 ($n=6$)

Fig 2 Effect of D-gal on VSMCs cell activity ($n=6$)

* $P < 0.05$, ** $P < 0.01$, vs. 0 mg/mL group.

组, D-gal组VSMCs中Cx43蛋白表达量降低($P < 0.01$); AAP10组VSMCs中Cx43蛋白表达量高于D-gal组($P < 0.01$)。

2.5 各组VSMCs细胞上P16、P21蛋白的表达及分布情况

见图4~图6。由Western blot及细胞免疫荧光实验结果可以看出, 相比于对照组, D-gal组VSMCs上P16的

蛋白表达升高($P < 0.01$), P21的蛋白表达量也升高($P < 0.01$), AAP10预处理细胞后再给予D-gal干预时, P16及P21的表达较D-gal组都有所下降($P < 0.01$), 且P16、P21均在细胞核上强表达, 给予AAP10预处理细胞后再给予D-gal干预, 可以明显降低P16、P21在细胞核上的表达。

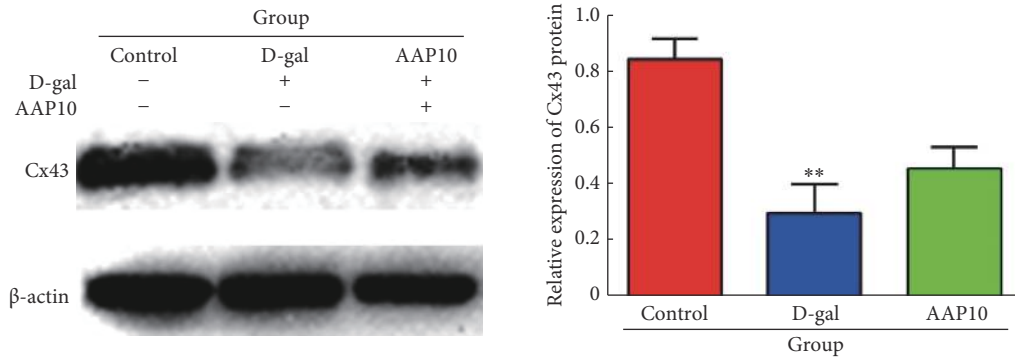


图 3 D-gal对VSMCs上Cx43蛋白表达的影响 (n=6)

Fig 3 Effect of D-gal on Cx43 protein expression in VSMCs (n=6)

** $P < 0.01$, vs. control group and AAP10 group.

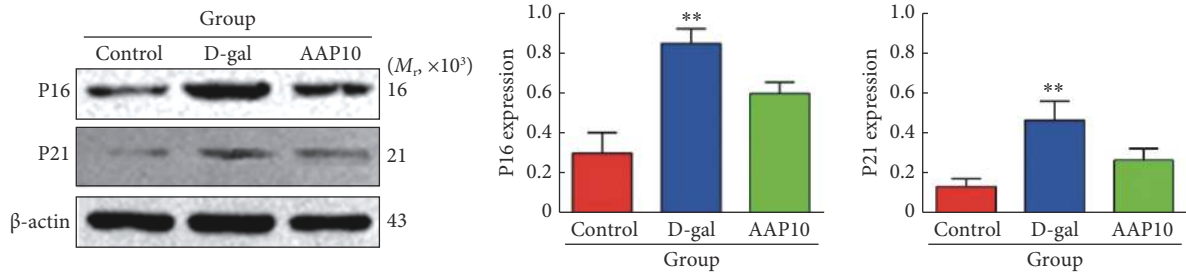


图 4 D-gal对VSMCs上P16、P21蛋白表达的影响 (n=6)

Fig 4 Effect of D-gal on P16 and P21 protein expression in VSMCs (n=6)

** $P < 0.01$, vs. that of the control group and AAP10 group.

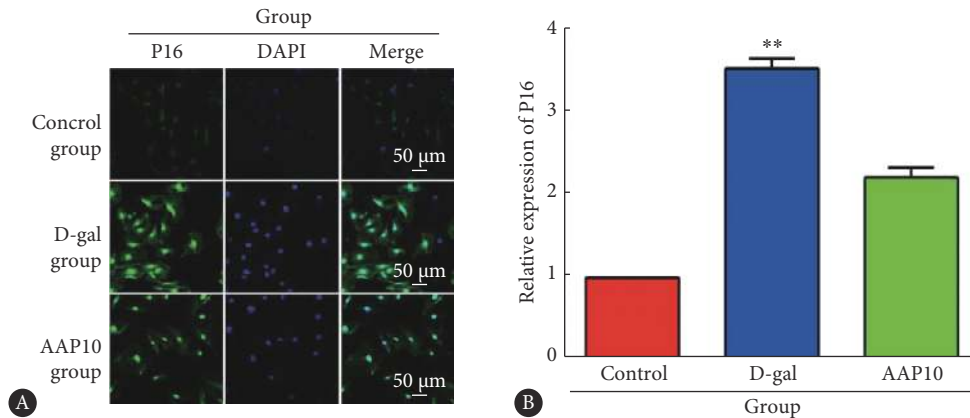


图 5 D-gal对VSMCs上P16蛋白表达分布的影响

Fig 5 Effect of D-gal on P16 protein expression and distribution in VSMCs

A: Fluorescence staining diagram (×200), expression of P16 in VSMCs (green fluorescence); DAPI staining labeled nuclei (showing blue fluorescence); B: Quantitative histogram (n=6), ** $P < 0.01$, vs. control group and AAP10 group.

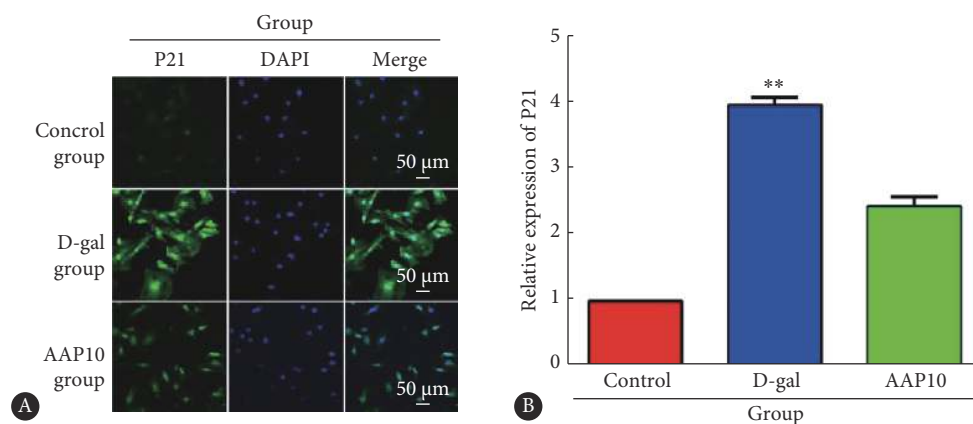


图 6 D-gal对VSMCs上P21蛋白表达的影响

Fig 6 Effect of D-gal on P21 protein expression and distribution in VSMCs

A: Fluorescence staining diagram ($\times 200$), expression of P21 in VSMCs (green fluorescence); DAPI staining labeled nuclei (showing blue fluorescence); B: Quantitative histogram ($n=6$), $**P<0.01$, vs. control group and AAP10 group.

3 讨论

在机体衰老过程中,常伴随听力的进行性下降^[6]。年龄相关性听力损失(AHL)是指伴随着年龄的增长,听力阈值逐渐增加的疾病^[1,7-8]。SMA是供应耳蜗循环系统的唯一动脉^[9],它与其它动脉一样均由VSMCs和内皮细胞构成,在维持血管正常生理功能方面具有重要的意义^[10]。组成血管壁的VSMCs、内皮细胞以及这两种细胞间均存在着大量的缝隙连接,它可以保证机械活动和血管电活动同步进行,维持血管正常生理功能及整体稳定性^[11-12]。实验证明,内皮细胞将超极化信息通过缝隙连接传递给VSMCs,进而引起肠系膜动脉产生舒张反应^[13]。Cx是缝隙连接通道和半通道的基本结构单位^[2]。有文献报道^[14],在血管壁上主要表达的蛋白有Cx40等多种缝隙连接蛋白,其中Cx43表达量最高,且在大鼠主动脉上Cx37、Cx40和Cx43的表达量随着年龄的增加逐渐降低^[13,15]。Cx26、Cx31与耳蜗内电位形成密切相关,内耳组织中Cx26分布表达最多,特异性敲除耳蜗上皮缝隙连接系统Cx26基因,可造成听力损伤^[16-17]。但目前有关SMA上Cx43表达与细胞衰老的研究尚无报道。

D-gal是一种常用的致衰老诱导剂,除制备动物衰老模型外^[18],还被应用于诱导体外细胞衰老模型。负性细胞周期调节蛋白P16、P21被认为是与衰老相关的重要蛋白,二者是细胞G₁/S期转换的重要因素,在动物衰老和细胞衰老过程中具有不可替代的重要作用^[19-20]。为了客观直接地反映耳蜗螺旋动脉VSMCs Cx43随衰老的变化情况,本实验对耳蜗螺旋动脉VSMCs进行原代培养,将VSMCs用D-gal诱导制备细胞衰老模型,检测各组细胞Cx43、P16及P21表达变化,进一步说明Cx43与衰老的关

系。本次实验的结果表明,D-gal可造成VSMCs衰老,P16、P21蛋白表达明显上升;在给予AAP10预处理,接着再给予D-gal进行干预后,发现可以在促进Cx43表达的同时抑制P16及P21蛋白的表达,说明Cx43在耳蜗螺旋动脉VSMCs的衰老中发挥重要作用,且上调Cx43蛋白的表达可能会延缓细胞衰老的发生。

综上所述,D-gal诱导的SMA衰老伴随SMA上Cx43表达下降,通过上调Cx43的表达可以逆转衰老相关蛋白P16和P21的表达异常。提示Cx43可能参与了D-gal诱导的耳蜗螺旋动脉VSMCs衰老,为临床上延缓细胞衰老提供了可靠的理论依据以及可能的药物干预靶点。

参 考 文 献

- [1] TU N C, FRIEDMAN R A. Age-related hearing loss: unraveling the pieces. *Laryngoscope Investig Otolaryngol*, 2018, 3(2): 68-72.
- [2] LAIRD D W, NAUS C C, LAMPE P D. SnapShot: Connexins and disease. *Cell*, 2017, 170(6): 1260-1260.
- [3] FFIGUEROA X F, ISAKSON B E, DULING B R. Connexins: gaps in our knowledge of vascular function. *Physiology*, 2004, 19(5): 277-284.
- [4] HAGEN A, DIETZE A, DHEIN S. Human cardiac gap-junction coupling: effects of antiarrhythmic peptide AAP10. *Cardiovasc Res*, 2009, 83(2): 405-409.
- [5] MEI L, CHEN J, ZONG L, *et al*. A deafness mechanism of digenic Cx26 (GJB2) and Cx30 (GJB6) mutations: reduction of endocochlear potential by impairment of heterogeneous gap junctional function in the cochlear lateral wall. *Neurobiol Dis*, 2017, 108: 195-198.
- [6] XIAO J J, YANG R, QIN X Q, *et al*. A role of AMPK and connexin 43 in the suppression of CoCl₂-induced apoptosis of spiral modiolar artery smooth muscle cells by adiponectin. *Life Sci*, 2019, 238: 116876[2021-01-23]. <https://doi.org/10.1016/j.lfs.2019.116876>.
- [7] YUAN J, ZHAO X Y, HU Y J, *et al*. Autophagy regulates the degeneration of the auditory cortex through the AMPK-mTOR-ULK1 signaling

- pathway. *Int J Mol Med*, 2018, 41(4): 2086–2098.
- [8] GAO F, WANG G B, MA W, *et al.* Decreased auditory GABA+ concentrations in presbycusis demonstrated by edited magnetic resonance spectroscopy. *Neuroimage*, 2015, 106: 311–316.
- [9] REIMANN K, KRISHNAMOORTHY G, WIER W G, *et al.* Gender differences in myogenic regulation along the vascular tree of the gerbil cochlea. *PLoS One*, 2011, 6(9): e25659[2011-1-23]. <https://doi.org/10.1371/journal.pone.0025659>.
- [10] REIMANN K, KRISHNAMOORTHY G, WANGEMANN P. NOS inhibition enhances myogenic tone by increasing rho-kinase mediated Ca^{2+} sensitivity in the male but not the female gerbil spiral modiolar artery. *PLoS One*, 2013, 8: e53655[2019-12-03]. <https://doi.org/10.1371/journal.pone.0053655>.
- [11] MILKAU M, KOHLER R, DE WIT C. Crucial importance of the endothelial K^+ channel SK3 and Connexin40 in arteriolar dilations during skeletal muscle contraction. *FASEB J*, 2010, 24(9): 3572–3579.
- [12] MATCHKOV V V. Mechanisms of cellular synchronization in the vascular wall. Mechanisms of vasomotion. *Dan Med Bull*, 2010, 57(10): B4191[2019-12-03]. <https://pubmed.ncbi.nlm.nih.gov/21040688/>.
- [13] 付勇南, 王梦洪. 缝隙连接和高血压. *中华高血压杂志*, 2008, 16(5): 397–399.
- [14] LI L, MA K T, ZHAO L, *et al.* Niflumic acid hyperpolarizes smooth muscle cells via calcium-activated potassium channel in spiral modiolar artery of guinea pigs. *Acta Pharmacol Sin*, 2008, 29: 789–799.
- [15] ABRAMS C K, SCHERER S S. Gap junctions in inherited human disorders of the central nervous system. *Biochim Biophys Acta*, 2012, 1818(8): 2030–2047.
- [16] LAUTERMANN J, TEN CATE W J, ALTENHOFF P, *et al.* Expression of the gap-junction Connexins 26 and 30 in the rat cochlea. *Cell Tissue Res*, 1998, 294(3): 415–420.
- [17] SUN J, AHMAD S, CHEN S, *et al.* Cochlear gap junctions coassembled from Cx26 and 30 show faster intercellular Ca^{2+} signaling than homomeric counterparts. *Am J Physiol Cell Physiol*, 2005, 288(3): C613–C635.
- [18] 司超, 张治平, 范志茹, 等. 耳蜗螺旋动脉上连接蛋白43与老年性耳聋的关系研究. *中国全科医学*, 2019, 22(27): 3339–3346.
- [19] AAHANGARPOUR A, NAJIMI S A, FARBOOD Y. Effects of Vitex agnus-castus fruit on sex hormones and antioxidant indices in a D-galactose-induced aging female mouse model. *J Chin Med Assoc*, 2016, 79(11): 589–596.
- [20] 李轶, 刘会占, 龚树生, 等. 耳蜗毛细胞与血管纹的相互依存关系的研究. *中华耳科学杂志*, 2014(3): 475–480.

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