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胶质细胞源性神经营养因子在肠道炎症性疾病中作用的研究进展

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Role of glial cell line-derived neurotrophic factor in intestinal inflammatory diseases

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Abstract

Glial cell line-derived neurotrophic factor (GDNF), a member of the neurotrophic factor family, promotes the survival, proliferation, migration, differentiation, and axonal growth of intestinal neurons. With studies on the role that enteric glia cells (EGCs) play in intestinal inflammation, GDNF has come into vision as an anti-inflammatory factor in the gut. Recent studies have gradually witnessed that, besides the role in protecting the intestinal epithelial barrier, GDNF plays an important part in a variety of protective mechanisms against intestinal inflammation, and has become the focus of numerous defense mechanisms in intestinal inflammation. GDNF also plays a very important role in the occurrence and development of intestinal inflammatory diseases. This review summarizes the results of recent studies in this field to fully discuss the roles of GDNF in the occurrence and development of intestinal inflammatory diseases.

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Key Words: Glial cell line-derived neurotrophic factor; Enteric nervous system; Enteric glia cells

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摘要

胶质细胞源性神经营养因子(glial cell line-

■背景资料

胶质细胞源性神经营养因子(Glial cell line-derived neurotrophic factor, GDNF)自从1993年被纯化和克隆以来,逐步受到人们的重视,并很快发现了他在增强脑多巴胺能神经元的存活、营养神经和促进多巴胺能神经元成熟分化等方面的作用。近年来,随着对肠神经胶质细胞(enteric glia cells, EGCs)研究的深入, GDNF又成为EGCs发挥其生物功能的重要执行者,再度引起人们的重视。

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目前,已基本明确GDNF可以通过促进已破坏肠上皮细胞增殖、加强肠上皮间的细胞连接和抗肠上皮细胞凋亡等途径保护肠上皮屏障的完整性。并且,亦有部分证据表明GDNF可以通过干预增殖平滑肌与ENS修复的平衡体系抑制肠道炎症的进展。然而,如何应用GDNF的这些功能特征有效的干预肠道炎症性疾病的进程仍需进一步的研究。

derived neurotrophic factor, GDNF)是神经营养因子家族中的一员,在肠道发挥着促进肠神经元存活、增殖、迁移、分化和轴突生长的作用。随着肠神经胶质细胞(enteric glia cells, EGCs)在肠道炎症中所发挥作用研究的深入, GDNF又以一个肠道抗炎因素的身份进入人们的视野。并且,在近年来的研究中, GDNF从一个EGCs保护肠道上皮屏障的参与者逐渐演变成成为多种肠道炎症保护机制中的重要角色,成为重重肠道炎症防御机制中的焦点。在肠道炎症性疾病的发生和发展中, GDNF同样扮演着非常重要的角色。本文总结近年来该领域的研究成果,力求全面地反映GDNF在肠道炎症性疾病发生发展的过程中所发挥的作用。

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关键词: 胶质细胞源性神经营养因子; 肠神经系统; 肠神经胶质细胞

核心提示: 胶质细胞源性神经营养因子(Glial cell line-derived neurotrophic factor, GDNF)是由多种细胞分泌的能够参与肠道炎症反应的一种神经营养因子,他在肠道的多个层面发挥着抗炎作用,人为干预和应用GDNF可能有助于肠道炎症性疾病的治疗。

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0 引言

肠道炎症性疾病涉及范围较广,一般来说是累及回肠、直肠、结肠的肠道炎症。其中,部分肠道炎症性疾病的发病机制尚未完全明确,例如炎症性肠病(inflammatory bowel disease, IBD),其病因涉及感染^[1]、环境^[2]、免疫^[3]、遗传^[4]和精神因素^[5]等多个方面。近年来,对肠神经系统(enteric nervous system, ENS)在肠道炎症过程中所发挥作用的诸多研究使得肠道炎症发生时肠道各种防御机制的作用过程日趋清晰。例如,肠神经胶质细胞(enteric glia cells, EGCs)在肠道炎症发生时发挥着保护肠黏膜屏障完整性的作用^[6,7];经典Wnt途径在IBD大鼠肌间神经丛的ENS细胞中处于激活状态并参与炎症过程,发挥着抗炎和促炎的双重作用^[8];肠道炎症时,增殖的肠平滑肌细胞与肠道神经元

的修复间存在相互作用,共同构建了抵御肠道炎症进展的又一道防线^[9]。然而,这些肠道炎症的防御机制都与一种物质密切相关-胶质细胞源性神经营养因子(Glial cell line-derived neurotrophic factor, GDNF)。GDNF通过GDNF/GFR α 1/RET复合体发挥其生物功能^[10,11],成为肠道炎症过程的多个防御体系的重要介质,甚至直接作用肠上皮、平滑肌及肠神经细胞,维护肠道结构和功能的完整性。

1 GDNF及其受体在肠道所发挥的生理作用

GDNF是转化生长因子 β (transforming growth factor-beta, TGF- β)超家族的一个远亲成员,是一个由134个氨基酸残基组成的一种糖基化的并由二硫键键合的同型二聚体。最早于1993年由Lin等^[12]纯化和克隆,他们发现GDNF能够增强脑多巴胺能神经元的存活,具有强力的营养神经和促进多巴胺能神经元成熟分化的作用,但并未改变神经元和神经胶质细胞的数量。

1.1 GDNF家族及其受体 GDNF、人神经肽蛋白(neurturin, NRTN)、PSPN(persephin)、ARTN(artemin)共同组成GDNF家族配体(GDNF family ligands, GFLs)^[13]。其中GDNF、NRTN和ARTN支持中央、周围和自主神经元群的存活,而PSPN只支持几个中央神经元群的存活^[14]。他们都是通过激活RET/GFR α 受体复合物发挥其生物功能, GDNF结合GFR α 1^[15], NRTN结合GFR α 2^[16], ARTN结合GFR α 3^[17]、PSPN结合GFR α 4^[18]。在某些情况下GDNF/GFR α 2和ARTN/GFR α 1形成复合物发挥特定的生物学功能^[19]。

1.2 肠道中GDNF的分布及来源 GDNF存在于大多哺乳动物的肠道。Peters等^[20]的研究显示,在成年大鼠的胃肠道中, GDNF在食道和胃组织中浓度最低,在肠道的浓度较高,而分离的肠肌壁组织中GDNF的含量是完整肠组织的4倍。在人类的空肠和结肠中也可以检测到较高浓度的GDNF。传统的观点认为, EGCs是肠道中GDNF的唯一来源^[21]。随着研究的深入,人们发现肠道中GDNF亦可来源于肠道的其他细胞。Han等^[9]对成年Balb/c小鼠的研究表明增殖的结肠环形平滑肌细胞可以分泌GDNF。Meir等^[22]在肠上皮细胞系CACO2和HT29B6的Western中检测到显著量的GDNF表达。Maruccio等^[23]对猫胎儿阶段的研究发现肠

■ 相关报道

Xiao等阐述了GDNF在急性缺血再灌注损伤条件下对肠道上皮细胞的保护作用。Zhang等表示, GDNF在体内可通过抑制髓过氧化物酶(myeloperoxidase, MPO)活性,降低白介素-1 β (interleukin-1 β , IL-1 β)和肿瘤坏死因子- α (tumour necrosis factor- α , TNF- α)的表达,增加ZO-1和Akt的表达发挥抗上皮细胞凋亡和降低肠上皮通透性的功效。

上皮细胞表达GDNF的同时表达嗜铬粒蛋白(chromogranin, CG). 这些结果暗示GDNF可能广泛表达于肠道的多种细胞.

1.3 GDNF在肠道中发挥的生理作用 ENS是存在于肠道肌层间的相互交联的神经丛, 他被认为是外周神经系统中最大和最复杂的部分^[24]. ENS主要由两部分组成: 肠神经元(enteric neurons cells, ENC)和EGCs. EGCs在维持肠道组织完整性和调节肠神经活动方面发挥着重要作用^[25,26]. GDNF作为EGCs分泌的神经营养因子之一在EGCs执行生理功能的过程中发挥着重要作用^[27]. GDNF通过GDNF/RET信号调节ENS发育的各个环节, 包括存活、增殖、迁移和肠神经元的分化^[10]. GDNF/RET缺陷型小鼠显示出肠神经元缺乏以及肾发育不全^[28,29]. 而Sprouty1、Sprouty2、KIF26A和NEDL2在GDNF/RET途径中发挥调节作用^[30-33]. GDNF在肠道炎症及其他损伤状态下发挥着更加突出的作用.

2 GDNF在肠道炎症过程中的作用

由于GDNF在肠神经元的生长和肠道上皮组织完整性的维持方面都发挥着重要作用, 因此, GDNF对肠道炎症的发生具有抑制作用. 同时, 在肠道炎症发生和发展的过程中, GDNF通过多条途径发挥抗炎作用.

2.1 GDNF通过直接保护肠上皮屏障发挥抗炎作用 GDNF在肠上皮发挥着促进上皮细胞增殖、成熟, 抑制上皮细胞凋亡以及加强上皮细胞间连接的作用. Meir等^[22]在体外实验中发现重组GDNF对CACO2和HT29B6细胞应用24 h能够显著的改善未成熟单层上皮细胞的屏障功能. 并且在伤口愈合实验中发现体外应用重组GDNF的损伤区域出现更快的肠上皮细胞增殖. 进一步的研究表明, 由EGCs和肠上皮细胞共同分泌的GDNF通过与GFR α /RET形成复合体激活cAMP/PKA途径促进上皮细胞增殖, 通过p38丝裂原活化蛋白激酶(mitogen-activated protein kinase, MAPK)途径介导未成熟肠上皮细胞的分化和成熟上皮细胞的屏障功能. Steinkamp等^[34]的研究表明GDNF能够有效抑制肿瘤坏死因子相关凋亡诱导配体(tumor necrosis factor-related apoptosis-inducing ligand, TRAIL)诱导的SW480细胞凋亡, 这种抗肠上皮细胞凋亡作用主要通过MAPK和PI3K/Akt途径

介导. 此外, 我们之前在葡聚糖硫酸钠(dextran sulphate sodium, DSS)诱导的小鼠结肠炎模型中应用GDNF的实验表明: GDNF在体内通过抑制髓过氧化物酶(myeloperoxidase, MPO)活性, 降低白介素-1 β (interleukin-1 β , IL-1 β)和肿瘤坏死因子- α (tumour necrosis factor- α , TNF- α)的表达, 增加的ZO-1和Akt的表达发挥抗上皮细胞凋亡和降低肠上皮通透性的功效^[35]. 总之, GDNF从多个方面发挥着保护肠道上皮屏障的作用, 守卫着抵御肠道炎症及损伤的第一道防线.

2.2 GDNF通过保护EGCs抗凋亡自分泌环路发挥抗炎作用 EGCs对肠道动力^[36]和肠上皮屏障^[37]均有调节功能. 1998年, Bush等^[38]诱导的EGCs缺陷小鼠出现黏膜屏障完整性丧失、通透性增加、产生肠道炎症、出血及坏死等IBD的表现, 证实了EGCs在肠上皮稳态中发挥着调控作用. 此后, Savidge等^[39]证实EGCs可以通过释放S-亚硝基谷胱甘肽(S-nitrosoglutathione, SNOG)保护肠黏膜屏障并减轻炎症. 随着研究的进一步深入, 人们发现EGCs既能分泌保护肠黏膜屏障的介质, 如SNOG、GDNF^[35]、神经生长因子(nerve growth factor, NGF)^[40]、TGF- β ^[41]等. 又能分泌iNOS/NO^[42]、15dPGJ2^[43]等抑制肠上皮细胞增殖、增加肠黏膜通透性的因子. 在肠道炎症初期, EGCs网络既发挥着抗炎作用, 同时又受到炎症的侵害. von Boyen等^[44]研究发现CD患者不发炎的结肠组织EGCs网络破坏严重甚至无GDNF表达. 这一病理进程严重影响EGCs抗炎作用的发挥, 能否抑制EGCs网络的破坏也成为遏制CD病程进展的关键. 新近, Steinkamp等^[45]发现在CD患者EGCs中存在一条依赖GDNF释放的抗凋亡自分泌环路, 该抗凋亡机制可以有效地抑制EGCs网络的破坏. 换言之, GDNF可以通过EGCs的自分泌环路抑制EGCs自身的凋亡, 从而间接的发挥抗炎作用.

2.3 GDNF通过对ENS的修复和干预间接发挥抗炎作用 生理条件下, GDNF调节ENS生长的各个环节. 在肠道炎症过程中, GDNF通过对ENS的修复及干预ENS的抗炎途径发挥抗炎作用. 肠道炎症过程中ENS的完整性遭到破坏, 除EGCs网络破坏外, 肠神经元的轴突变性和肠神经元坏死相继发生^[9]. 肠道正常分泌及蠕动功能受到影响, 继发炎症进展. 而GDNF

■ 创新盘点

本文总结了近年来有关GDNF在肠道炎症性疾病发生、发展过程中所发挥作用的多数研究成果, 从肠道结构的多个层面系统的阐述了GDNF在肠道炎症性疾病的多个病程中所发挥的作用.

应用要点

本文丰富了人们对肠道炎症性疾病发病机制的理解, 明确了GDNF在肠道炎症进程的各个阶段所扮演的角色, 为今后对GDNF的进一步研究指明了方向, 同时也为肠道炎症性疾病的诊治提供了新的思路。

在肠道炎症环境下发挥着促进损伤的神经轴突再生和髓鞘化的作用^[46,47], 保证了肠神经元结构和功能的完整性, 从而为抵御肠道炎症损伤发挥正性作用。另外, Wnt蛋白家族(Wnt family proteins, Wnts)在肠上皮稳态中发挥着重要作用^[48]。经典的Wnt在ENS细胞中表达活跃, 并通过Wnt/ β -catenin通路对促炎因素激活的NF- κ B发挥负调节作用^[8], 而GDNF、碱性成纤维细胞生长因子(basic fibroblast growth factor, bFGF)和NGF能够促进G蛋白偶联Frizzled受体-9(G protein-coupled receptor Frizzled 9, FZD9)的表达, 从而增强Wnt/ β -catenin信号, 发挥抗炎作用。

2.4 GDNF通过干预增殖平滑肌与ENS修复的平衡体系发挥抗炎作用 GDNF在肠道不仅作用于肠上皮, 维持肠上皮屏障的形态和功能, 在肠道炎症进展的过程中还可以作用于增殖平滑肌与重新分布的ENS之间的平衡, 进一步发挥抵御炎症损伤的作用。肠道炎症引起的肠神经轴突变性和神经元死亡, 导致部分肠肌层缺乏神经支配, 甚至逐渐造成肠道平滑肌细胞(intestinal smooth muscle cells, ISMC)的损害, 但随后便出现ISMC的增殖^[49]和肠神经轴突的生长并导致肠神经的重新支配^[50]。在上述过程中, 处于增殖阶段的ISMC能够表达GDNF, 促进神经轴突的再生并介导神经元及其轴突在新生的肠道平滑肌中重新支配^[9]。反过来, 成功的再支配往往会抑制ISMC的继续增殖, 从而恢复肠道的收缩功能^[51]。然而在诸如IBD等慢性反复的肠道炎症性疾病中, 上述机制可能被打破。反复破坏和增殖的ISMC可能失去GDNF的表达能力进而失去神经再支配的能力, 而ISMC的持续增生也将导致肠腔狭窄及运动障碍^[52]。总之, 在肠道炎症病程突破上皮损伤肌层的过程中, GDNF依然间接发挥着抗炎作用。但如何使得这种抗炎机制持续存在仍需要进一步的研究。

3 结论

GDNF在肠道的多个防御层面和多种防御机制中发挥着抗炎作用, 已然成为肠道抗炎因素的核心。然而, 在肠道炎症的病理进程中, 由于GDNF来源细胞的破坏和表达体系的缺失导致他在多个环节中抗炎作用的削减, 外加促炎因素的加强、免疫防御体系的破坏等多方面原

因, 最终引发炎症的蔓延。如何把握肠道炎症疾病的病理进程, 并在机体抗炎防御的各个层面有效的应用GDNF或促进GDNF的表达从而达到遏制或扭转肠道炎症的病理进程的效果将成为我们今后的研究方向。

4 参考文献

- Li Y, Xia X, Zhang J, Song Z, Zhou L, Zhang Y, Huang Y, Shi Y, Quigley EM, Ding S. Haemophagocytic lymphohistiocytosis in inflammatory bowel disease with virus infection. *Prz Gastroenterol* 2015; 10: 78-82 [PMID: 26557937 DOI: 10.5114/pg.2015.48995]
- Aujnarain A, Mack DR, Benchimol EI. The role of the environment in the development of pediatric inflammatory bowel disease. *Curr Gastroenterol Rep* 2013; 15: 326 [PMID: 23640032 DOI: 10.1007/s11894-013-0326-4]
- Di Giovangiulio M, Verheijden S, Bosmans G, Stakenborg N, Boeckstaens GE, Matteoli G. The Neuromodulation of the Intestinal Immune System and Its Relevance in Inflammatory Bowel Disease. *Front Immunol* 2015; 6: 590 [PMID: 26635804 DOI: 10.3389/fimmu.2015.00590]
- Bianco AM, Girardelli M, Tommasini A. Genetics of inflammatory bowel disease from multifactorial to monogenic forms. *World J Gastroenterol* 2015; 21: 12296-12310 [PMID: 26604638 DOI: 10.3748/wjg.v21.i43.12296]
- Triantafyllidis JK, Merikas E, Gikas A. Psychological factors and stress in inflammatory bowel disease. *Expert Rev Gastroenterol Hepatol* 2013; 7: 225-238 [PMID: 23445232 DOI: 10.1586/egh.13.4]
- Savidge TC, Sofroniew MV, Neunlist M. Starring roles for astroglia in barrier pathologies of gut and brain. *Lab Invest* 2007; 87: 731-736 [PMID: 17607301 DOI: 10.1038/labinvest.3700600]
- Van Landeghem L, Chevalier J, Mahé MM, Wedel T, Urvil P, Derkinderen P, Savidge T, Neunlist M. Enteric glia promote intestinal mucosal healing via activation of focal adhesion kinase and release of proEGF. *Am J Physiol Gastrointest Liver Physiol* 2011; 300: G976-G987 [PMID: 21350188 DOI: 10.1152/ajpgi.00427.2010]
- Di Liddo R, Bertalot T, Schuster A, Schrenk S, Tasso A, Zanusso I, Conconi MT, Schäfer KH. Anti-inflammatory activity of Wnt signaling in enteric nervous system: in vitro preliminary evidences in rat primary cultures. *J Neuroinflammation* 2015; 12: 23 [PMID: 25644719 DOI: 10.1186/s12974-015-0248-1]
- Han TY, Lourenszen S, Miller KG, Blennerhassett MG. Intestinal smooth muscle phenotype determines enteric neuronal survival via GDNF expression. *Neuroscience* 2015; 290: 357-368 [PMID: 25655216 DOI: 10.1016/j.neuroscience.2015.01.056]
- Heanue TA, Pachnis V. Enteric nervous system development and Hirschsprung's disease: advances in genetic and stem cell studies. *Nat Rev Neurosci* 2007; 8: 466-479 [PMID: 17514199 DOI: 10.1038/nrn2137]
- Enomoto H. Regulation of neural development by glial cell line-derived neurotrophic factor family ligands. *Anat Sci Int* 2005; 80: 42-52 [PMID: 15811111 DOI: 10.1007/s12265-005-5555-5]

- 15794130 DOI: 10.1111/j.1447-073x.2005.00099.x]
- 12 Lin LF, Doherty DH, Lile JD, Bektesh S, Collins F. GDNF: a glial cell line-derived neurotrophic factor for midbrain dopaminergic neurons. *Science* 1993; 260: 1130-1132 [PMID: 8493557]
- 13 Wang X. Structural studies of GDNF family ligands with their receptors-Insights into ligand recognition and activation of receptor tyrosine kinase RET. *Biochim Biophys Acta* 2013; 1834: 2205-2212 [PMID: 23085183 DOI: 10.1016/j.bbapap.2012.10.008]
- 14 Baloh RH, Enomoto H, Johnson EM, Milbrandt J. The GDNF family ligands and receptors - implications for neural development. *Curr Opin Neurobiol* 2000; 10: 103-110 [PMID: 10679429]
- 15 Goodman KM, Kjær S, Beuron F, Knowles PP, Nawrotek A, Burns EM, Purkiss AG, George R, Santoro M, Morris EP, McDonald NQ. RET recognition of GDNF-GFR α 1 ligand by a composite binding site promotes membrane-proximal self-association. *Cell Rep* 2014; 8: 1894-1904 [PMID: 25242331 DOI: 10.1016/j.celrep.2014.08.040]
- 16 Demir IE, Wang K, Tieftrunk E, Giese NA, Xing B, Friess H, Kehl T, Ceyhan GO. Neuronal plasticity in chronic pancreatitis is mediated via the neurturin/GFR α 2 axis. *Am J Physiol Gastrointest Liver Physiol* 2012; 303: G1017-G1028 [PMID: 22961804 DOI: 10.1152/ajpgi.00517.2011]
- 17 Thornton P, Hatcher JP, Robinson I, Sargent B, Franzén B, Martino G, Kitching L, Glover CP, Anderson D, Forsmo-Bruce H, Low CP, Cusdin F, Dosanjh B, Williams W, Steffen AC, Thompson S, Eklund M, Lloyd C, Chessell I, Hughes J. Artemin-GFR α 3 interactions partially contribute to acute inflammatory hypersensitivity. *Neurosci Lett* 2013; 545: 23-28 [PMID: 23603259 DOI: 10.1016/j.neulet.2013.04.007]
- 18 Yang J, Lindahl M, Lindholm P, Virtanen H, Coffey E, Runeberg-Roos P, Saarma M. PSPN/GFR α 4 has a significantly weaker capacity than GDNF/GFR α 1 to recruit RET to rafts, but promotes neuronal survival and neurite outgrowth. *FEBS Lett* 2004; 569: 267-271 [PMID: 15225646 DOI: 10.1016/j.febslet.2004.06.007]
- 19 Sariola H, Saarma M. Novel functions and signalling pathways for GDNF. *J Cell Sci* 2003; 116: 3855-3862 [PMID: 12953054 DOI: 10.1242/jcs.00786]
- 20 Peters RJ, Osinski MA, Hongo JA, Bennett GL, Okragly AJ, Haak-Frendscho M, Epstein ML. GDNF is abundant in the adult rat gut. *J Auton Nerv Syst* 1998; 70: 115-122 [PMID: 9686911]
- 21 张德奎, 甘华田. 重视研究肠道神经系统在炎症性肠病发病中作用. *世界华人消化杂志* 2008; 16: 3200-3203
- 22 Meir M, Flemming S, Burkard N, Bergauer L, Metzger M, Germer CT, Schlegel N. Glial cell line-derived neurotrophic factor promotes barrier maturation and wound healing in intestinal epithelial cells in vitro. *Am J Physiol Gastrointest Liver Physiol* 2015; 309: G613-G624 [PMID: 26294673 DOI: 10.1152/ajpgi.00357.2014]
- 23 Maruccio L, D'Angelo L, de Girolamo P, Lucini C, Castaldo L. GDNF and GFR α co-receptor family in the developing feline gut. *Ann Anat* 2014; 196: 296-302 [PMID: 24834895 DOI: 10.1016/j.aanat.2014.03.001]
- 24 Benarroch EE. Enteric nervous system: functional organization and neurologic implications. *Neurology* 2007; 69: 1953-1957 [PMID: 17998487 DOI: 10.1212/01.wnl.0000281999.56102.b5]
- 25 Bassotti G, Villanacci V, Fisogni S, Rossi E, Baronio P, Clerici C, Maurer CA, Cathomas G, Antonelli E. Enteric glial cells and their role in gastrointestinal motor abnormalities: introducing the neuro-gliopathies. *World J Gastroenterol* 2007; 13: 4035-4041 [PMID: 17696219]
- 26 von Boyen GB, Steinkamp M, Geerling I, Reinshagen M, Schäfer KH, Adler G, Kirsch J. Proinflammatory cytokines induce neurotrophic factor expression in enteric glia: a key to the regulation of epithelial apoptosis in Crohn's disease. *Inflamm Bowel Dis* 2006; 12: 346-354 [PMID: 16670534 DOI: 10.1097/01.MIB.0000219350.72483.44]
- 27 Hansebout CR, Su C, Reddy K, Zhang D, Jiang C, Rathbone MP, Jiang S. Enteric glia mediate neuronal outgrowth through release of neurotrophic factors. *Neural Regen Res* 2012; 7: 2165-2175 [PMID: 25538736 DOI: 10.3969/j.issn.1673-5374.2012.028.001]
- 28 Sánchez MP, Silos-Santiago I, Frisé J, He B, Lira SA, Barbacid M. Renal agenesis and the absence of enteric neurons in mice lacking GDNF. *Nature* 1996; 382: 70-73 [PMID: 8657306 DOI: 10.1038/382070a0]
- 29 Schuchardt A, D'Agati V, Larsson-Blomberg L, Costantini F, Pachnis V. Defects in the kidney and enteric nervous system of mice lacking the tyrosine kinase receptor Ret. *Nature* 1994; 367: 380-383 [PMID: 8114940 DOI: 10.1038/367380a0]
- 30 Basson MA, Akbulut S, Watson-Johnson J, Simon R, Carroll TJ, Shakra R, Gross I, Martin GR, Lufkin T, McMahon AP, Wilson PD, Costantini FD, Mason IJ, Licht JD. Sprouty1 is a critical regulator of GDNF/RET-mediated kidney induction. *Dev Cell* 2005; 8: 229-239 [PMID: 15691764 DOI: 10.1016/j.devcel.2004.12.004]
- 31 Taketomi T, Yoshiga D, Taniguchi K, Kobayashi T, Nonami A, Kato R, Sasaki M, Sasaki A, Ishibashi H, Moriyama M, Nakamura K, Nishimura J, Yoshimura A. Loss of mammalian Sprouty2 leads to enteric neuronal hyperplasia and esophageal achalasia. *Nat Neurosci* 2005; 8: 855-857 [PMID: 15937482 DOI: 10.1038/nn1485]
- 32 Zhou R, Niwa S, Homma N, Takei Y, Hirokawa N. KIF26A is an unconventional kinesin and regulates GDNF-Ret signaling in enteric neuronal development. *Cell* 2009; 139: 802-813 [PMID: 19914172 DOI: 10.1016/j.cell.2009.10.023]
- 33 Wei R, Qiu X, Wang S, Li Y, Wang Y, Lu K, Fu Y, Xing G, He F, Zhang L. NEDL2 is an essential regulator of enteric neural development and GDNF/Ret signaling. *Cell Signal* 2015; 27: 578-586 [PMID: 25555806 DOI: 10.1016/j.cellsig.2014.12.013]
- 34 Steinkamp M, Geerling I, Seufferlein T, von Boyen G, Egger B, Grossmann J, Ludwig L, Adler G, Reinshagen M. Glial-derived neurotrophic factor regulates apoptosis in colonic epithelial cells. *Gastroenterology* 2003; 124: 1748-1757 [PMID:

■名词解释

肠神经胶质细胞 (EGCs): 是包裹在肠神经元细胞体、轴突束和肠血管外的一种“星形”外观的小细胞, 是在肠神经系统中丰富的细胞类型, 他们在肠道形成EGCs网络, 对于肠道神经元的支撑、发育、分化和存活都有重要作用。

同行评价

本文选题较新颖, 对GDNF在肠道抗炎中的作用机制进行了总结分析, 为肠道炎症性疾病的治疗和预防提供了新的思路。

- 12806607]
- 35 Zhang DK, He FQ, Li TK, Pang XH, Cui de J, Xie Q, Huang XL, Gan HT. Glial-derived neurotrophic factor regulates intestinal epithelial barrier function and inflammation and is therapeutic for murine colitis. *J Pathol* 2010; 222: 213-222 [PMID: 20632386 DOI: 10.1002/path.2749]
- 36 Bassotti G, Villanacci V, Antonelli E, Morelli A, Salerni B. Enteric glial cells: new players in gastrointestinal motility? *Lab Invest* 2007; 87: 628-632 [PMID: 17483847 DOI: 10.1038/labinvest.3700564]
- 37 齐国卿, 谢瑞霞, 张德奎. 肠神经胶质细胞在炎症性肠病发生发展中作用的研究进展. *世界华人消化杂志* 2014; 22: 1076-1080
- 38 Bush TG, Savidge TC, Freeman TC, Cox HJ, Campbell EA, Mucke L, Johnson MH, Sofroniew MV. Fulminant jejuno-ileitis following ablation of enteric glia in adult transgenic mice. *Cell* 1998; 93: 189-201 [PMID: 9568712]
- 39 Savidge TC, Newman P, Pothoulakis C, Ruhl A, Neunlist M, Bourreille A, Hurst R, Sofroniew MV. Enteric glia regulate intestinal barrier function and inflammation via release of S-nitrosoglutathione. *Gastroenterology* 2007; 132: 1344-1358 [PMID: 17408650 DOI: 10.1053/j.gastro.2007.01.051]
- 40 von Boyen GB, Steinkamp M, Reinshagen M, Schäfer KH, Adler G, Kirsch J. Nerve growth factor secretion in cultured enteric glia cells is modulated by proinflammatory cytokines. *J Neuroendocrinol* 2006; 18: 820-825 [PMID: 17026531 DOI: 10.1111/j.1365-2826.2006.01478.x]
- 41 Neunlist M, Aubert P, Bonnaud S, Van Landeghem L, Coron E, Wedel T, Naveilhan P, Ruhl A, Lardeux B, Savidge T, Paris F, Galmiche JP. Enteric glia inhibit intestinal epithelial cell proliferation partly through a TGF-beta1-dependent pathway. *Am J Physiol Gastrointest Liver Physiol* 2007; 292: G231-G241 [PMID: 16423922 DOI: 10.1152/ajpgi.00276.2005]
- 42 Xiao W, Wang W, Chen W, Sun L, Li X, Zhang C, Yang H. GDNF is involved in the barrier-inducing effect of enteric glial cells on intestinal epithelial cells under acute ischemia reperfusion stimulation. *Mol Neurobiol* 2014; 50: 274-289 [PMID: 24878766 DOI: 10.1007/s12035-014-8730-9]
- 43 Bach-Ngohou K, Mahé MM, Aubert P, Abdo H, Boni S, Bourreille A, Denis MG, Lardeux B, Neunlist M, Masson D. Enteric glia modulate epithelial cell proliferation and differentiation through 15-deoxy-12,14-prostaglandin J2. *J Physiol* 2010; 588: 2533-2544 [PMID: 20478974 DOI: 10.1113/jphysiol.2010.188409]
- 44 von Boyen GB, Schulte N, Pflüger C, Spaniol U, Hartmann C, Steinkamp M. Distribution of enteric glia and GDNF during gut inflammation. *BMC Gastroenterol* 2011; 11: 3 [PMID: 21235736 DOI: 10.1186/1471-230X-11-3]
- 45 Steinkamp M, Gundel H, Schulte N, Spaniol U, Pflueger C, Zizer E, von Boyen GB. GDNF protects enteric glia from apoptosis: evidence for an autocrine loop. *BMC Gastroenterol* 2012; 12: 6 [PMID: 22251670 DOI: 10.1186/1471-230X-12-6]
- 46 Madduri S, Papaloizos M, Gander B. Synergistic effect of GDNF and NGF on axonal branching and elongation in vitro. *Neurosci Res* 2009; 65: 88-97 [PMID: 19523996 DOI: 10.1016/j.neures.2009.06.003]
- 47 Zhang L, Ma Z, Smith GM, Wen X, Pressman Y, Wood PM, Xu XM. GDNF-enhanced axonal regeneration and myelination following spinal cord injury is mediated by primary effects on neurons. *Glia* 2009; 57: 1178-1191 [PMID: 19170182 DOI: 10.1002/glia.20840]
- 48 Gregorieff A, Pinto D, Begthel H, Destrée O, Kielman M, Clevers H. Expression pattern of Wnt signaling components in the adult intestine. *Gastroenterology* 2005; 129: 626-638 [PMID: 16083717 DOI: 10.1016/j.gastro.2005.06.007]
- 49 Alexander MR, Owens GK. Epigenetic control of smooth muscle cell differentiation and phenotypic switching in vascular development and disease. *Annu Rev Physiol* 2012; 74: 13-40 [PMID: 22017177 DOI: 10.1146/annurev-physiol-012110-142315]
- 50 Lourenssen S, Wells RW, Blennerhassett MG. Differential responses of intrinsic and extrinsic innervation of smooth muscle cells in rat colitis. *Exp Neurol* 2005; 195: 497-507 [PMID: 16098965 DOI: 10.1016/j.expneurol.2005.06.012]
- 51 Pelletier AM, Venkataramana S, Miller KG, Bennett BM, Nair DG, Lourenssen S, Blennerhassett MG. Neuronal nitric oxide inhibits intestinal smooth muscle growth. *Am J Physiol Gastrointest Liver Physiol* 2010; 298: G896-G907 [PMID: 20338922 DOI: 10.1152/ajpgi.00259.2009]
- 52 Nair DG, Han TY, Lourenssen S, Blennerhassett MG. Proliferation modulates intestinal smooth muscle phenotype in vitro and in colitis in vivo. *Am J Physiol Gastrointest Liver Physiol* 2011; 300: G903-G913 [PMID: 21311027 DOI: 10.1152/ajpgi.00528.2010]

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