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评 述

硒和硒蛋白与宿主肠道健康的互作调节机制

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摘要 硒是生物体必需的微量元素之一, 在体内合成为硒蛋白, 参与抗氧化和免疫应答等众多生理机能的调控. 近期研究表明, 硒和硒蛋白可能与宿主肠道微生物、抗氧化系统和免疫因子存在互作调节肠道稳态的功能, 进而起到预防和治疗肠道疾病的作用. 本文综述了硒在肠道中的吸收和硒蛋白的合成及功能, 重点解析了硒和硒蛋白与肠道微生物、肠道氧化应激和肠道免疫间的互作调节机制及其在肠癌中的潜在作用, 以期为硒用于预防或治疗肠道疾病提供新的思路和依据.

关键词 硒, 硒蛋白, 肠道微生物, 氧化应激, 免疫, 癌症

硒于1817年被瑞典科学家Berzelius最先发现, 并在1957年被确定为人体必需的微量营养元素[1]. 作为一种维持生命健康的基本元素, 硒在人体内主要通过25种硒蛋白的表达发挥其生物学作用[2]. 先前研究主要聚焦于硒水平与人类疾病如克山病与大骨节病的关系解析[3,4]. 新近研究越来越关注硒与肠道健康, 发现硒不仅可通过调节肠道细胞的氧化还原状态、炎症信号通路及免疫细胞功能缓解氧化应激和炎症反应, 而且还可通过增强肠道上皮细胞之间的紧密连接以维持肠黏膜屏障功能[5]. 此外, 硒和硒蛋白可介导肠道微生物与宿主之间的相互作用[6,7], 肠道菌群也能反过来影响硒的生物利用度和硒蛋白在肠道内的表达, 促进硒的吸收与利用[8,9]. 多项研究表明, 肠道菌群紊乱和肠道氧化应激极易发展为肠道炎症, 而长期的慢性炎症与氧化应激状态又极大概率会恶化为肠癌, 机体补硒可预防和治疗肠癌[10~12]. 由此可见, 硒在维持肠道功能和促进肠道健康方面有至关重要的作用. 然而, 目前鲜有硒与肠道功能互作调节研究的相关综述. 因此, 本文简述了硒在肠道中的吸收和硒蛋白的合成及功能, 重点解析了硒和硒蛋白与肠道微生物、肠道氧化应激和肠道免疫间的互作调节机制, 探讨了硒在预防和治疗肠癌中的潜在作用, 以期为硒用于预防或治疗

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常见肠道疾病提供新的思路和依据.

1 硒的吸收与硒蛋白的合成、种类及功能

硒主要存在于水、空气和土壤中, 并借助植物和微生物的摄取从而进入食物链[13,14]. 自然界中硒一般以两种形式存在: 无机硒和有机硒. 有机硒, 如硒代蛋氨酸(selenomethionine, SeMet)和硒代半胱氨酸(selenocysteine, SeCys或Sec), 是通过钠依赖的转运系统在小肠内被吸收[15,16]. 而无机硒, 如硒酸盐, 可穿过肠道刷状缘膜并借助硫酸盐的作用, 利用钠离子驱动的能量转运系统进行吸收; 此外, 亚硒酸盐还可通过无载体介导的被动扩散作用在肠道内被吸收[17~20]. 研究表明, 硒代蛋氨酸肠道吸收率约为96%, 而亚硒酸盐仅约为40%; 与硒酸盐与亚硒酸盐的肠道吸收率相比, 亚硒酸盐的吸收率大约只有硒酸盐的一半[21,22]. 虽然无机硒也能在肠道内被很好地吸收, 但是动物更倾向于吸收有机硒, 并且有机硒的生物利用度比无机硒更高[23]. 硒在肠道内被吸收后, 可通过血液循环进入肝脏代谢, 或被特定的硒转运载体(如硒蛋白P, (selenoprotein P, SelP))转运到目标组织发挥其生理学功能.

硒代半胱氨酸被认为是第21种编码氨基酸, 由UGA密码子编码, 在硒蛋白的合成及其功能发挥过程中发挥重要作用[24]. 硒酸盐或亚硒酸盐形式的硒在机体内会被谷胱甘肽、硫氧还蛋白以及谷氧还蛋白还原为硒化氢[25]. 同时, 外源摄入的硒代半胱氨酸被β裂解酶裂解后可得到硒化氢, 硒代蛋氨酸可以通过γ裂解酶的作用转化为甲基硒醇, 然后进一步转化为硒化氢(图1). 硒化氢作为硒蛋白合成的重要底物被硒蛋白硒磷酸合成酶2(selenophosphate synthetase 2, SPS2)转化为硒磷酸, 并进一步与Seryl-tRNA$^{[Ser]Sec}$反应形成Sec-tRNA$^{[Ser]Sec}$[26,27]. 随后Sec-tRNA$^{[Ser]Sec}$在硒代半胱氨酸插入序列结合蛋白(selenocysteine insertion sequence binding protein 2, SBP2)、特殊延伸因子(eEFsec)、硒蛋白硒磷酸合成酶1(SPS1)、核糖体蛋白L30、核糖体蛋白eS31和可溶性肝抗原蛋白的作用下, 在mRNA的3′端非翻译区形成一个可识别的独特二级结构, 进而将Sec插入正在延长的肽链中翻译成为成熟的硒蛋白[24,28,29]. 先前研究普遍认为, 硒蛋白催化还原反应行使其抗氧化功能是依靠其内部的硒代半胱氨酸残基发挥作用, 然而, 硒代半胱氨酸残基在不同硒蛋白中的具体功能至今尚未得到证实[30].

早在20年前就有学者提出在硒蛋白合成过程中应关注Sec插入的机制和效率[31]. UGA的翻译效率、SBP2活性、核糖体功能等常被认为是硒蛋白合成的限速点[31]. 最新研究发现, 特定的膳食营养也能影响硒蛋白的合成与表达[32]. 例如, 膳食硒的添加可以增加蛋鸡[33]、育肥猪[34]、肉牛[35]和羔羊[36]体内硒蛋白的表达量. Schwarz等人[37]也发现, 铜可能通过限制UGA的编码来影响硒蛋白的合成; Long等人[38]发现, 日粮添加丝氨酸可以调节硒蛋白的表达. 然而, 硒蛋白合成过程中的生物化学功能很多尚未深入解析, 例如tRNASec与SBP2何时何地如何解除核糖体, 以及Seryl-tRNA如何识别tRNA$^{[Ser]Sec}$及其相互作用的过程都尚不清楚, 因此, 硒蛋白合成效率的研究仍处于起步阶段[39,40].

目前发现人体内存在25种硒蛋白(小鼠为24种), 它们的生理功能主要是通过减少过氧化氢和脂质氧化物等过氧化物的含量来发挥抗氧化作用[5,41], 调控细胞增殖、凋亡和铁死亡[42~44], 辅助RNA转录与蛋白质折叠[45], 调节免疫细胞功能[46], 促进肌纤维分化[47]和提高精子活力[48]等. 由于硒蛋白的这些生物功能已在近期相关综述中进行了总结[49,50], 本文不再详细展开论述. 但截至目前, 仍存在少量硒蛋白功能不明确, 大部分硒蛋白功能了解不彻底的现象, 需要进一步研究和探索. 最新研究发现, 谷胱甘肽过氧化物酶2(glutathione peroxidase 2, GPX2)、硫氧还蛋白还原酶2(thioredoxin reductase 2, TR2)、硒蛋白S(selenoprotein S, SelS)和SelP与肠道稳态和肠道疾病息息相关, 其表达失常往往可导致肠道氧化应激、肠道炎症甚至肠癌的发生[49~51], 从而影响动物或人体肠道健康.

2 硒与肠道氧化应激

Schwarz等人[52]在1957年首次提出硒是一种潜在的抗氧化剂, 它表现出与维生素E相似的抗氧化作用. 研究表明, 一半以上的硒蛋白都具有抗氧化功能[50]. 这些硒蛋白中大多数在其酶活性位点上都包含一个或几个Sec, 并利用此Sec发挥氧化还原反应的催化作用[53]. 活性氧、丙二醛(malondialdehyde, MDA)、蛋白羰基等细胞氧化代谢产物含量的升高是细胞发生氧化应激的重要指标, 而机体可以利用体内存在的一些抗氧化剂来抵消这些代谢物产生的不利影响[54]. 生物

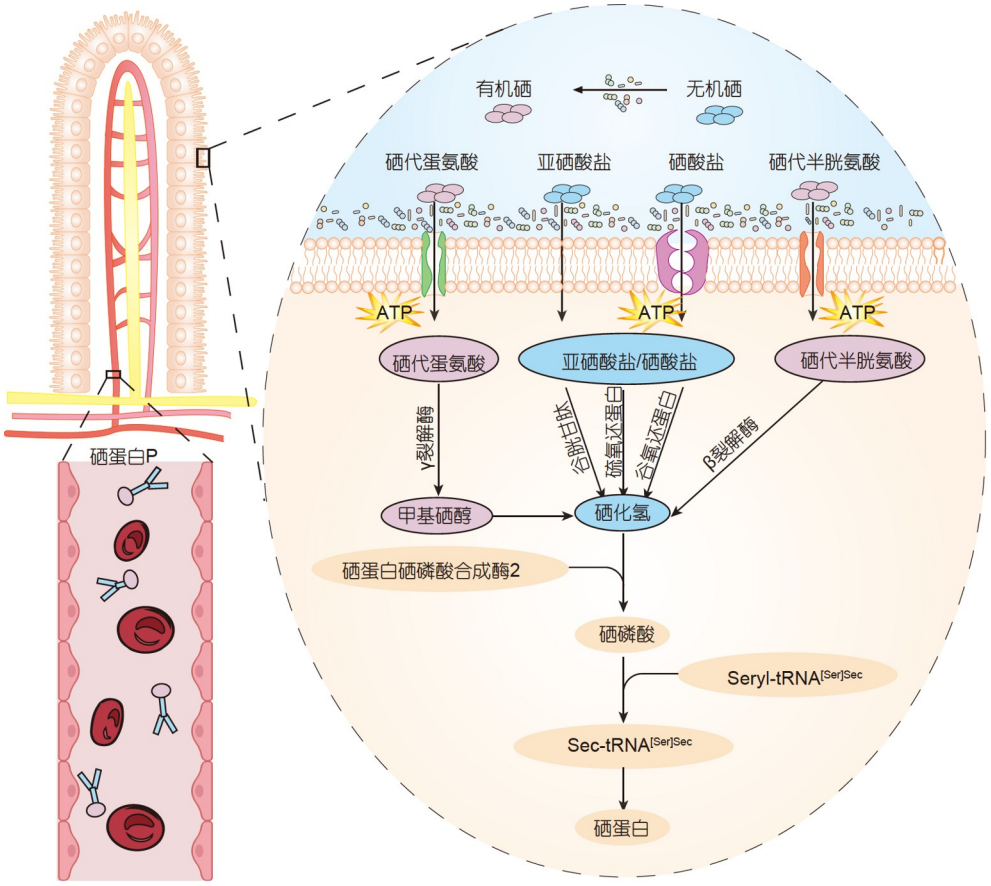

图 1　硒和硒蛋白在肠道中的吸收、合成与转运

Figure 1　The absorption, synthesis and transfer of selenium and selenoprotein in gut

体内的抗氧化系统可以分为酶促抗氧化剂和非酶促抗氧化剂. 常见的酶促抗氧化剂有超氧化物歧化酶(superoxide dismutase, SOD)、过氧化氢酶(catalase, CAT)、GPX和TR; 常见的非酶促抗氧化剂有谷胱甘肽、NADPH、硫氧还蛋白、维生素C和E等[55]. 其中, GPX和TR属于硒蛋白, 这两种硒蛋白在对抗肠道氧化应激的过程中起着不可替代的作用, 而GPX又被誉为抗氧化系统的“基石”[55,56]. 由于硒是通过硒蛋白来发挥其生理活性的, 硒蛋白的功能严重依赖于硒的参与, 因此硒的缺乏会显著影响GPX的抗氧化功能[57~59]. 机体主要有四种GPX在肠道中表达. GPX1几乎在所有类型的肠道细胞中表达; GPX2主要表达于肠道黏膜的上皮细胞和帕内特细胞中; GPX3主要在分泌型肠细胞中表达并能在血浆中被大量检测到; GPX4则多表达于肠道上皮细胞和固有层细胞中[60~65]. 此外, 四种GPX之间也存在相互协调的功能关系, 比如肠道内表达最多的GPX2, 其缺乏可以通过增加GPX1来补偿, 但如果同时缺乏GPX1和GPX2则会导致肠道抗氧化系统受损从而严重损害肠道健康[45].

核因子E2相关因子2(nuclear factor erythroid 2-related factor 2, Nrf2)与硒对肠道上皮细胞的保护作用密切相关[66,67]. 有研究表明, 硒可通过激活小鼠肠上皮细胞Nrf2信号从而发挥其抗氧化作用[68~70]. Nrf2是一种氧化应激传感器, 可通过改变其下游抗氧化相关基因的表达来调节抗氧化能力[71]. 在正常情况下, Kelch样环氧氯丙烷相关蛋白1(Kelch-like ECH-associated protein 1, Keap1)与Nrf2结合并存在于细胞质中. 在氧化应激条件下, 氧自由基会改变Keap1的结构并松弛其与Nrf2的结合, 游离的Nrf2可以进入细胞核并与抗氧化/电子反应元件(antioxidant response element/elec-

trophile response element, ARE/EpRE)结合, 从而增加包括GPX和TR在内的抗氧化基因的表达[72]. 研究发现, 刺激Nrf2的分泌可以促进硒蛋白的表达并增强结肠癌细胞Caco-2的抗氧化能力[73]. 此外, Qiao等人[7]研究发现, 硒可通过调节Nrf2介导的NLRP3信号通路来维持肠道菌群稳态, 并缓解小鼠肠道的氧化应激.

近年来, 许多学者发现添加不同形式的硒, 如无机硒[6,74]、有机硒[75,76]、纳米硒[77,78]和生物硒[79~81], 都能在不同程度上发挥缓解肠道氧化应激的作用. 总的来说, 生物硒和纳米硒对肠道的保护效果最好, 其次是有机硒, 最后是无机硒. Zhu等人[79]发现, 饲喂富硒双歧杆菌DD98可以提高血浆中SOD, GPX和SelP水平, 显著改善小鼠肠道氧化应激; Yang等人[80]发现, 饲喂富硒酵母可以减少MDA, 提高GSH含量与SOD活性, 有效地抑制肉鸡盲肠组织的氧化损伤; Wu等人[81]发现, 饲喂富硒嗜酸乳杆菌可以通过调节细胞炎症因子和肠道微生物群来改善葡聚糖硫酸钠(dextran sulphate sodium, DSS)处理后小鼠肠道中的氧化应激. 然而, 在上述研究中无法确定发挥主要作用的是硒还是其载体, 因为双歧杆菌和乳酸杆菌同样具有缓解肠道氧化应激和维持肠道健康的作用[82~84]. 因此, 生物硒缓解肠道氧化应激的作用机制还存在一定争议. 此外, 硒作为抗氧化利器, 其有效摄入量及安全剂量对机体生理功能至关重要, 目前对此剂量范围还未有具体定论.

3 硒与肠道微生物

肠道微生物作为肠道屏障的重要组成部分, 在维持肠道稳态和促进肠道健康方面发挥着不可或缺的作用. 肠道微生物与宿主之间对于硒的利用存在着错综复杂的互作关系[9]. 首先, 肠道微生物会限制宿主对硒的利用来影响宿主体内的硒水平与硒蛋白的表达[8,85]. 当肠道内的硒水平过低时, 肠道菌群会与宿主竞争硒; 当肠道内的硒水平较高, 甚至达到毒性剂量时, 肠道菌群可以帮助宿主消耗掉多余的硒以达到解毒的目的[86,87]. 在肠道内, 大约有四分之一的微生物在摄取硒后可以表达其自身的硒蛋白. 因此, 它们通常会与宿主竞争硒来满足自身的生长需要. 而当宿主硒不足时, 肠道微生物又可以将自身合成的硒蛋白分泌到肠腔内供宿主吸收利用[8,9]. 因此, 一方面肠道菌群对硒的“竞争性”摄取, 会增加宿主对硒元素的需求, 同时也会降低硒在宿主体内的利用率; 另一方面肠道菌群对硒的“保护性”摄取, 会减轻硒元素对宿主的毒性. 因此, 肠道微生物既能以“硒池”的形式为肠道筑起一条“护城河”, 也能像“城墙”一样保护肠道黏膜免受硒的毒性攻击.

食物中含有各种形式的含硒化合物, 这一部分硒可以被肠道微生物转化为SeMet或SeCys, 为机体提供一种生物利用度更高的硒化合物. Zhu等人[88]研究发现, 人体粪便中的富硒双歧杆菌可以高效地将无机硒转化为有机硒, 进而提高硒的生物利用率; Zhang和Pessione等人[89,90]发现, 特定的乳酸菌可以富集硒元素, 将亚硒酸钠以SeMet或SeCys的形式储存在细菌体内, 间接为宿主提供更易吸收的硒. 然而, 目前研究虽已发现部分肠道菌种具有富集和转化硒的能力, 但具体转化机制仍不清楚.

硒与肠道微生物之间的互作不仅包括肠道微生物对硒的影响, 同时还包括硒对肠道微生物的调控. 膳食硒可影响肠道微生物的整体多样性以及肠道微生物的定殖, 进而影响肠道健康[77,79~81,91]. Zhai等人[6]研究表明, 硒缺乏显著增加了小鼠肠道中*Dorea*菌种的水平. *Dorea*常见于肠易激综合征患者的肠道内, 其丰度增加提示肠道健康可能会受到不利影响[92]. 研究还发现, 低硒饮食的小鼠肠道内更容易出现伤寒沙门氏菌感染, 且更容易诱发结肠炎, 而日粮中补充硒能促进肠道有益菌的定殖, 减少肠道有害菌的生长, 增加肠道微生物的多样性[6]. Zhai等人[6]还发现, 高硒组的小鼠肠道中*Turicibacter*和阿克曼氏菌的数量显著增加, *Mucispirillum*的数量显著降低, *Turicibacter*具有潜在的抗炎活性, 阿克曼氏菌在保护宿主肠道屏障、免疫和代谢稳态中发挥重要作用, 而*Mucispirillum*的增加常与蠕虫感染有关[93~96], 表明高硒日粮可使小鼠抗炎和免疫功能更强. Molan等人[97]研究表明, 饲粮中添加含硒提取物能显著增加大鼠盲肠中的乳酸杆菌和双歧杆菌的数量, 减少大肠杆菌和沙门氏菌的数量. Wu等人[81]研究表明, 富硒嗜酸乳杆菌能显著增加结肠炎小鼠有益菌*Parasutterella*的相对丰度, 降低有害菌*Romboutsia*的相对丰度, 同时增加肠道菌群的β多样性. Li等人[98]研究表明, 饲粮中添加硒降低了肠道中副拟杆菌科和普雷沃氏菌科微生物的数量, 增加了厚壁菌门、瘤胃球菌科和考拉杆菌属微生物的数量. 综上所述, 硒可以通过改善肠道菌群的组成和丰度以保障肠道屏障功能, 从而促进肠道健康.

4　硒与肠道免疫

近年来, 越来越多的证据表明, 肠道炎症的发生可能与体内硒和硒蛋白的水平紧密关联[2,55,99]. 肠道炎症, 如炎症性肠病(inflammatory bowel disease, IBD)患者中通常伴随严重的氧化应激、肠道微生物失调和肠道免疫功能异常现象[100,101], 因此, 缓解肠道氧化应激、改善肠道菌群区系和加固肠道免疫系统将有助于IBD的预防与治疗[102~105]. 硒作为一种公认的抗氧化剂, 可以通过硒蛋白的作用显著减轻肠道内的氧化应激, 进而缓解肠道炎症并在一定程度上减少IBD的发生[5,55,99]. 大量实验证明, GPX2和SelP在减轻IBD患者肠道氧化应激的过程中至关重要[2,61,106]. 此外, TR1不仅可以降低IBD期间肠道的氧化应激水平, 还可以通过减少还原性连四硫酸盐来改善肠道微生物组成, 从而缓解肠道炎症[107]. 虽然有些研究表明, 硒可通过改善肠道微生物的组成来缓解肠道炎症[55], 但是参与介导硒缓解肠道炎症的关键菌群及其代谢物还有待进一步研究.

硒还可通过影响免疫细胞的数量与功能, 调控炎症信号通路和调节炎症因子的表达与分泌来改善肠道免疫功能. 研究表明, 先天性免疫细胞(如巨噬细胞)仅在硒蛋白表达时才会响应炎症刺激, 并减少促炎介质的表达[81,108]. 硒蛋白的存在是巨噬细胞和其他免疫细胞发挥抗炎作用的一个关键因素, 其潜在机制是硒蛋白具有将花生四烯酸代谢从促炎介质前列腺E2(prostaglandin E2, PGE2)转变为抗炎介质前列腺素D2(prostaglandin D2, PGD2)的能力[109]. 同时, 硒还可以促进巨噬细胞从M1向M2转化, 从而抑制炎症的发展[108]. 硒可以增加中性粒细胞和$CD4^+CD25^+$ T细胞的丰度, 降低γδT细胞, $CD4^+$, $CD4^+CD44^+$和$CD4^+CD69^+$ T细胞的丰度. 通过增加$CD4^+CD25^+$ Treg细胞的数量, 硒可抑制DSS诱导的结肠炎小鼠中促炎细胞因子的产生[110]. 小鼠缺硒会导致其在感染肠炎后的死亡率更高, 而膳食硒可以通过增加ILC3和Th17细胞来缓解肠炎[109]. 此外, 硒可通过调节白介素(interleukin, IL)、干扰素(interferon, IFN)和组织坏死因子(tumor necrosis factor, TNF), 如IL-1β, IL-2, IL-6, IL-8, IL-10, IL-17, IL-21, IFN-γ, TNF-α和TGF-β等诸多炎症因子表达或分泌, 从而发挥缓解肠道炎症的作用[81,98,111~113]. 核因子-κB(nuclear factor-κB, NF-κB)和过氧化物酶体增殖物激活受体γ(peroxisome proliferator-activated receptor γ, PPARγ)是研究最多的两种介导硒作用的信号通路. 硒可直接抑制IκB蛋白与NF-κB的解离, 也可以直接与NF-κB中的半胱氨酸硫醇相互作用, 从而抑制NF-κB的活化来缓解肠道炎症[109]. 此外, 硒可通过调节TLR4/MYD88信号通路, 抑制NF-κB的表达, 增加紧密连接相关基因*Claudin-1*, *Occludin*和*ZO-1*的表达, 拮抗氧化应激所引起的肠道屏障损伤[80]. PGD2属于一种PPARγ激动剂, 而硒可通过上调PGD2等产物在PPARγ的激活中起关键作用[114]. 在硒激活PPARγ的同时, 肠上皮细胞和巨噬细胞中的NF-κB失活, 从而减少炎性细胞因子的分泌并增加$Foxp3^+$ Treg细胞的分化[113]. 大量研究证明, 硒可以通过多个生理途径和信号通路来缓解肠道炎症, 降低IBD的发病率. 然而, 相关的作用机制以及硒应用于提高肠道免疫力, 预防和治疗常见肠道疾病过程中的安全性等问题还有待进一步研究和评估.

5　硒在肠癌中的潜在作用

70多年前, 科学家便发现硒可能具有预防癌症的作用[115]. 1977年, Jacobs等人[116]发现, 补充亚硒酸钠可减少结肠癌诱导大鼠的肿瘤数量. 自此, 大量实验证明膳食硒可减少结直肠癌细胞的增殖与迁移[99]. 流行病学研究表明, 硒缺乏会增加患癌症的风险, 而补充硒有利于多种癌症的预防[117]. 临床研究表明, 人体内硒水平与患结肠癌的风险与严重程度成反比, 硒摄入量越低的人群其结直肠癌死亡率越高[118]. 体外研究发现, 过量的硒会抑制人结直肠癌细胞的生长[119]. SelP主要存在于血浆中, 是一种硒蛋白转运载体. 近年来研究发现, 血清中SelP的水平与结肠癌发病率呈负相关[120], 表明血浆SelP可作为一种癌症发生的潜在标志物[99]. SelP可不依赖血浆供给而在肠细胞中内源分泌, 肠细胞分泌的SelP可抑制Wnt信号通路并减弱TNF-α和TGF-β的产生, 从而缓解炎症并抵抗肠癌[99]. 特异性敲除小肠细胞内的*SelenoP*会导致内源性SelP分泌减少和肠道内抗氧化环境发生改变, 显著促进肿瘤的形成[51].

肠道炎症与氧化应激如果不及时干预很大概率会发展为肠癌, 而硒抗癌的主要机制便是抗氧化和缓解炎症[10]. 研究表明, 肠炎患者患癌症的风险是非肠炎患者的6倍[121]. 炎症介质和通路如NF-κB, IL-6, IL-23,

转录激活因子(signal transducer and activator of transcription, STAT)和Th17一定程度上会阻碍细胞进入凋亡程序, 从而导致其过度增殖. 因此, 在这些介质或信号存在的情况下, 癌变概率的增加是不可避免的[122]. 此外, 在IBD患者中发现了Wnt信号通路的失调及其过度活跃, 且在IBD患者肿瘤的形成过程中观察到了Wnt甲基化, 而这些过程通常在散发性结直肠癌患者中也能观察到[123,124]. 研究表明, 高剂量的亚硒酸钠可抑制肿瘤的增大、组织的进一步癌变与癌症的扩散[12,125]. 硒可以减少由偶氮甲烷/葡聚糖硫酸钠(AOM/DSS)诱导以及在*ApcMin*遗传模型中诱导的结肠肿瘤的发生[126~129]. 利用AOM/DSS诱导小鼠发生结肠癌后, 硒可以加速肿瘤细胞的凋亡, 抑制其增殖. GPX在肠癌的发生过程中起着重要作用. 虽然有研究表明, 添加硒并不能阻止*GPX2*敲除小鼠癌症的发生, 但其肠道炎症会随着硒浓度的增加逐渐缓解, 且GPX2的抗癌作用主要归功其抗炎功效[127,130,131]. *GPX2*和*GPX1*双敲除会导致小鼠严重的结肠炎, 且会进一步癌变并产生恶性肿瘤[132,133]. 相似地, *GPX3*的敲除也增加了AOM/DSS结肠炎相关癌症模型中的肿瘤数量[121]. 细胞培养研究发现了硒抑制人类结直肠癌细胞的另一种辅助机制, 即硒可以激活依赖AMP的蛋白激酶, 随后阻碍细胞外调节激酶信号通路的传导从而减少肿瘤细胞的数量[134]. Huang等人[135]发现, 纳米硒可触发人结肠直肠细胞系的自噬, 这可能是硒抗肿瘤作用的另一作用机制. 也有研究发现硒可抑制COX-2的表达, 从而预防和治疗结直肠癌[134,136]. 总之, 大量研究表明, 硒可以通过减轻氧化应激, 缓解炎症和调控多个信号通路来预防肠癌.

虽然人类流行病学研究和动物疾病模型实验结果都支持硒具有强大的抗肿瘤作用, 但是大规模的人体临床试验结果却不尽如人意, 均未能证明补充硒与预防结直肠癌之间存在明确的联系[99]. 美国一项测试硒和维生素E在癌症预防与治疗效果的研究显示, 硒补充剂对结直肠癌没有保护效果[137]. 尽管有少数临床研究表明, 补充硒可降低患结直肠癌的风险, 但这种相关性并未显现出其普遍性[138~140]. 因此推测, 影响结直肠癌治疗效果的因素非常多, 硒只是其中一个因素, 其可作为具有治疗肠癌的潜在药物, 但癌症的治疗需要从多角度对症下药. 此外, 至于如何使膳食硒在体内转化成有效的“癌症杀手”, 又如何使“癌症杀手”们有效联合起来抗癌, 其中的复杂机制还需要深入研究.

6 总结与展望

近年来, 大量研究表明, 硒可通过调节肠道微生物, 减轻肠道氧化应激或缓解肠道炎症来改善肠道健康, 进而起到预防和治疗肠道相关疾病的作用. 然而, 这些研究的思路较为单一, 未考虑到肠道微生物、肠道氧化应激、肠炎与肠癌之间存在的密切联系, 应尽可能将这些重点要素在研究思路中串联起来, 更好地研究硒和硒蛋白在肠道方面的功能机制. 此外, 目前的研究还存在很多问题尚待解决. 例如, 影响硒和硒蛋白在肠道中吸收、合成与转化的相关因素, 肠道微生物与硒相互影响的具体机制, 硒作为药物治疗肠道疾病的安全性, 为什么硒在动物癌症模型中能起到很好的抗癌效果, 临床试验的结果却不尽如人意? 尽管这些问题还有待进一步研究与探讨, 但研究硒和硒蛋白在促进肠道健康的生物学效应方面具有广阔的前景和价值, 硒很有潜力成为肠癌治疗的关键性药物, 并且有望开发成保健品运用于肠道炎症的预防与肠道菌群紊乱的调控, 提高人体免疫力.

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Role of selenium and selenoprotein in gut health

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Selenium, one of the essential trace elements for living organisms, participates in the regulation of physiological functions such as anti-oxidation and immune response when converted into selenoproteins. Recent studies have shown that selenium and selenoproteins may interact with host intestinal microbiota, antioxidant system, and immune factors to regulate intestinal homeostasis, therefore played a crucial role in the prevention and treatment of intestinal diseases. In this review, the absorption of selenium in the intestinal tract and the synthesis and function of selenoproteins were briefly introduced, the interactive regulation mechanism of selenium and selenoproteins with intestinal microbiota, intestinal oxidative stress, and intestinal immunity were discussed, and the potential role of selenium in intestinal cancer were analyzed, which provided new ideas and basis for the use of selenium in the prevention or treatment of intestinal diseases.

selenium, selenoprotein, gut microbiota, oxidative stress, immunity, cancer

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