微生物学报
Acta Microbiologica Sinica
2016, 56(9): 1398-1405
http://journals.im.ac.cn/actamicrocn
DOI: 10.13343/j.cnki.wsxb.20150558

Mini-Review 小型综述

3-磷酸甘油醛脱氢酶在细菌粘附中的作用及机制

刘丽，章文明，王翀，汪海峰*

浙江农林大学动物科技学院，动物营养研究所，浙江 临安 311300

摘要： 3-磷酸甘油醛脱氢酶(GAPDH)是糖酵解中的关键酶，参与糖酵解过程，生成能量。除了这些基本功能，GAPDH还参与tRNA出核、催化微管聚合、调节蛋白质表达与磷酸化、参与自噬等多种其他生理功能。研究表明GAPDH在细菌的黏附中发挥重要作用。本文主要综述GAPDH的基本功能，及其黏附作用与其机制，最后展望了GAPDH研究与应用前景。

关键词： 3-磷酸甘油醛脱氢酶，粘附，机制，细菌

微生物在胃肠道的黏附和定殖是其发挥作用的首要条件，微生物及其成分与肠道免疫细胞、上皮细胞的相互作用是目前肠道粘膜免疫的一大研究热点。研究报道，微生物表面成分包括表面蛋白(Surface layer protein, Slp)、磷壁酸(Teichoic acid, TA)、胞外多糖(Exopolysaccharides, EPS)等在动物肠道粘膜黏附中发挥作用[1]。GAPDH是糖酵解途径中的1个关键酶，其基因作为管家基因，几乎在所有组织中都高水平表达，并且在同种细胞或组织中的表达量一般恒定，因而GAPDH在Western blotting等实验操作中常作为标准化的内参，以定量其他基因或者蛋白质的表达[2]。GAPDH不仅存在于细胞质、细胞膜和线粒体中[3]，同时分布在细胞表面而作为黏附分子，兼职发挥粘附作用。但是，GAPDH如何由细胞质转移到细胞外，在细胞膜上的黏附过程等都不甚明了。本文旨在综述GAPDH的基本功能和黏附作用，探讨微生物管家蛋白GAPDH发挥兼职黏附作用机制。

1 GAPDH的基本功能

研究表明，GAPDH作为糖酵解酶，除参与糖酵解外，还具有与RNA结合、催化微管聚合、调节蛋白质表达与磷酸化、参与自噬、亚硝基化核蛋白和招募转铁蛋白等多种其他生理功能。GAPDH的主要功能包括：(1) 糖酵解功能，催化3-磷酸甘油醛生成1，3-二磷酸甘油酸，同时将能量转移到高能磷酸键中[4]；(2) 参与tRNA的出核，研究表明，GAPDH能够与RNA结合，形成GAPDH-tRNA复合物，促进tRNA的转运出核[5]；

基金项目： 国家自然科学基金(31601951)；浙江省自然科学基金(Y14C170018)；国家星火计划(2015GA700001)

*通信作者。Tel/Fax：+86-571-63743313；E-mail：hfwang@zafu.edu.cn

收稿日期： 2015-11-22；**修回日期：** 2016-02-25；**网络出版日期：** 2016-02-29

(3) tRNA能够携带氨基酸，促使mRNA翻译形成蛋白质，所以GAPDH能够促进蛋白质的表达。已有研究表明，GAPDH调节组蛋白H_2B的表达[6]；(4) 参与DNA损伤修复，脱嘌呤/嘧啶核酸内切酶1 (apurinic/apyrimidimic endonudease 1，APE1)是DNA切除修复中的关键酶，GAPDH能还原氧化型的APE1，修复DNA损伤[7]。另外，GAPDH可与端粒结合，维持端粒长度，提高DNA的稳定性[8]；(5) 催化微管聚合，磷酸化的GAPDH能够高度亲和微管蛋白，催化微管聚合[9]；(6) 参与蛋白磷酸化修饰[10]，纯化的GAPDH在体外与ATP和Mg^{2+}孵育，通过酸沉淀在GAPDH中发现^{32}P，证实GAPDH还能自磷酸化[11]；(7) GAPDH参与膜融合和膜转运，通过检测一系列膜融合蛋白功能效应，发现GAPDH能够最有效的促进膜融合；(8) 促进细胞凋亡，在不换培养基但定期补给葡萄糖的情况下，进行大鼠小脑颗粒神经元体外培养，发现神经元不断凋亡，同时细胞凋亡时伴随GAPDH基因的过表达，表明GAPDH能够促进细胞凋亡[12]；(9) 亚硝基化的GAPDH能够使组蛋白去乙酰酶、DNA依赖性蛋白激酶和去乙酰化酶SIRT1亚硝基化，发挥细胞信号转导作用[13]；(10) GAPDH能招募转铁蛋白影响铁的吸收[14]。

除上述多种功能外，一些探索性研究还发现GAPDH参与多种疾病，增加GAPDH的表达能够增加乙型病毒相关的肝癌和肝硬化患者的存活率[15]。在肿瘤、糖尿病、亨廷顿病[16]和神经退行性疾病(阿尔兹海默症，帕金森病[17])等疾病中，GAPDH的表达量出现明显的增高或者降低，GAPDH这些新功能有待进一步解析。

2 细菌表面GAPDH的兼职粘附功能

研究发现，细菌细胞核、细胞质和细胞膜表面均分布有GAPDH，不同部位的GAPDH具有不同的作用[3]。作为兼职功能蛋白(protein moonlighting, gene sharing)，分布在细菌细胞膜上的GAPDH除了具有促进膜融合和膜转运的作用外，还具有粘附作用[18–19]。

Ramiah等[20]研究表明，用盐酸胍处理除去表面蛋白(GAPDH、EF-Tu、TPI)的乳酸杆菌在与人结肠癌细胞(CaCo-2)粘附时，黏附的细菌数与正常乳酸杆菌相比下降40%，说明细菌表面蛋白有助于乳酸杆菌与细胞的粘附。乳杆菌能够抑制病原菌的粘附，研究报道，詹氏乳杆菌(*Lactobacillus jensenii*)能够抑制淋病奈球菌对上皮细胞的黏附：将分别经甲醇和蛋白酶K处理的詹氏乳杆菌与淋病奈球菌同时加入上皮细胞中培养，发现经甲醇处理过的詹氏乳杆菌能够显著抑制淋病奈球菌黏附于上皮细胞表面，其抑制能力与野生型詹氏乳杆菌无差异，经蛋白酶k处理的詹氏乳杆菌抑制淋病奈球菌能力显著减弱，表明其黏附效应的物质具有蛋白活性。提取詹氏乳杆菌表面蛋白加入淋病奈球菌与上皮细胞共培养体系，发现细菌表面蛋白能抑制淋病奈球菌的黏附，抑制黏附能力与表面蛋白含量成正比。将提取的细菌表面蛋白纯化，发现了2个含量最高蛋白，其中一个是GAPDH，另一个是烯醇化酶[21]。Kinoshita等[22]通过生物传感器的方法证实植物乳酸杆菌的GAPDH能够黏附人类结肠粘液，通过等离子共振结合技术分析蛋白与蛋白的互作关系，发现植物乳酸杆菌GAPDH能够与人类结肠黏液中表达的A、B血型抗原结合。在GAPDH和人类结肠黏液孵育时加入NAD^+，发现GAPDH与人类结肠黏液的粘附性下降，表明GAPDH与NAD^+结合位点可能与人类结肠黏液的黏附有关[23]。除有益菌外，有害菌的GAPDH也具有粘附作用。研究发现，肠出血性大肠杆菌(enterohemorthagic, EHEC)和肠致病性大肠杆菌(enteropathogenic, EPEC)表面均存在GAPDH，但未发现非致病性大肠杆菌向胞外分泌GAPDH，EHEC和EPEC分泌的 GAPDH能够与人

类的纤溶酶原和纤维蛋白原结合，Caco-2上皮细胞经过EHEC和EPEC共孵育培养后，在上皮细胞上发现有粘附的GAPDH[24]。在脑膜炎奈瑟氏菌中，*GapA-1*基因是标记GAPDH基因之一，*GapA-1*基因缺陷的脑膜炎奈瑟氏菌与野生型细菌相比，能够显著减少与人脑微血管内皮细胞的黏附作用[25]。作者所在课题组提取鼠李糖乳酸杆菌细菌表面蛋白，发现乳酸杆菌的细菌表面蛋白能够抑制p38信号通路，减少炎性因子的产生[26]，有研究发现，阻断小肠上皮细胞黏附依赖性信号通路对小肠上皮细胞具有益生作用[27]，作者所在课题组得到的试验结果与其结果一致。对不同黏附力乳酸杆菌的表面蛋白提取后分析发现，高黏附力菌株的表面蛋白内含有GAPDH，将表面蛋白去除或用抗体封闭GAPDH后，菌体与猪小肠上皮细胞系IPEC-J2和人结肠癌细胞系Caco-2细胞的粘附能力下降，表明乳酸杆菌菌体表面的GAPDH参与黏附作用[19]。

3 GAPDH黏附作用的机制

有益菌和有害菌均可通过GAPDH介导与肠道细胞或者粘蛋白黏附而发挥有益或有害作用。不同细菌的GAPDH，结合的细胞成分不同，发挥不同的生理作用(表1)。当GAPDH与肌动蛋白、肌球蛋白、粘蛋白、层黏连蛋白或纤连蛋白结合时，发挥黏附作用[28]；当GAPDH与纤维蛋白原、尿激酶受体、纤溶酶原或纤溶酶结合时，发挥侵袭作用[18–29]；当GAPDH与小分子GTP蛋白结合酶Rab5a和内吞囊泡膜结合时，发挥吞噬作用[30]；当GAPDH与溶菌酶、补体和IL-10结合时，发挥免疫调节作用[28–31]。

表1. 不同细菌GAPDH结合的靶标

Table 1. GAPDH-binding targets in different strains

GAPDH-binding targets	Bacteria	Reference
Plasminogen/plasmin	*Bacillus anthracis*, *Escherichia coli*, *Lactobacillus plantarum*, *Streptococcus oralis*	[18–29]
Urokinase-type plasminogen activator receptor of human pharyngeal cell	*Streptococcus pyogenes*	[32]
Lysozyme	*Streptococcus pyogenes*	[28]
Actin	*Streptococcus pyogenes*, *Streptococcus agalactiae*	[28–33]
Myosin	*Streptococcus pyogenes*	[28]
Albumin	*Streptococcus suis*	[34]
Fibrinogen	*Streptococcus agalactiae*	[28]
Fibronectin	*Escherichia coli*, *Streptococcus pyogenes*	[35]
Intestinal epithelia	*Lactobacillus Plantarum*, *Escherichia coli*	[36]
Colon mucous, vaginal mucous	*Lactobacillus plantarum*, *Mycoplasma genitalium*	[22–36]
A and B blood group antigens	*Lactobacillus plantarum*	[23]
Complement	*Haemonchus contortus*	[31]

3.1 与粘蛋白结合

胃肠道上皮细胞持续接受物理、化学和生物刺激，容易遭受病原微生物及其产物的侵袭，粘膜上皮细胞通过多种机制来规避这种危害。粘膜上皮细胞分泌粘液，粘液中含有粘蛋白、抗体、溶菌酶、纤溶酶原和防御素等多种物质，组成了

一道保护上皮细胞的屏障。粘蛋白主要有膜结合型和分泌型2种形式[37]。粘液中的粘蛋白是分泌型粘蛋白，它含有富含苏氨酸、脯氨酸和丝氨酸残基的串联重复序列，在丝氨酸和苏氨酸序列中含有丰富的糖基化位点，蛋白质的糖基化作用影响粘蛋白的物理性质。粘蛋白上的寡糖能与多种物质结合，目前证实粘蛋白含有半乳糖和乙酰半乳糖，痢疾阿米巴原虫存在外源凝集素能够与半乳糖和乙酰半乳糖结合，粘附于黏液层[38]。霍乱弧菌则是通过蛋白GbpA与粘蛋白的N-乙酰葡萄糖胺结合，粘附于粘液上[39]。

Kinoshita等[22]发现经过磷酸缓冲盐溶液PBS (phosphate buffer saline)洗涤的乳酸菌与蒸馏水洗涤的乳酸菌相比，对人结肠粘液素(HCM)的粘附能力减弱，通过对PBS洗脱液进行SDS-PAGE电泳，检测到一个大约40 kDa的蛋白，通过序列分析，确定该蛋白是GAPDH。通过基于表面等离子共振的生物分析传感技术绘制出传感图，分析数据进一步证实GAPDH能与粘蛋白结合[22]。Glenting提取了乳酸杆菌*L. plantarum* strains 299v的表面蛋白，在分别包被有纤溶酶原、纤连蛋白和粘蛋白的微量滴定板中加入细菌表面蛋白，加入抗GAPDH的血清，再加入带有碱性磷酸酶标记的二抗，在405 nm波长下测其吸光光度值，该酶联免疫吸附反应实验结果证实GAPDH能够与纤溶酶原、纤连蛋白和粘蛋白结合[18]。

3.2 与肌动蛋白和肌球蛋白结合

肌动蛋白是微丝的结构蛋白，肌动蛋白参与构成细胞骨架；肌球蛋白为肌原纤维粗丝的组成单位，存在于平滑肌中，在肌肉运动中起重要作用。一些细菌与粘蛋白粘附后，释放蛋白酶，细菌透过粘液屏障到达黏膜，粘附于粘膜上皮细胞中的肌球蛋白与肌动蛋白。先前研究证实，A型链球菌的M蛋白和脂磷壁酸参与细菌的黏附作用[40]，将细胞溶解酶对链球菌的溶解产物进行SDS-PAGE凝胶电泳，发现一个有别于M蛋白的39 kDa蛋白；纯化该蛋白，通过氨基酸序列比对分析发现该蛋白为GAPDH；分析GAPDH与6种不同蛋白的互作关系，结果发现GAPDH能与肌动蛋白和肌球蛋白结合[28]。

3.3 与层黏连蛋白、纤连蛋白和纤溶酶原结合

层黏连蛋白主要存在于上皮细胞基膜中，是基膜所特有的非胶原糖蛋白，作为基膜的主要结构成分对基膜的组装起关键作用。纤连蛋白广泛存在于动物组织和组织液中，介导细胞黏附。纤溶酶原是血浆纤维蛋白水解酶无活性的前体，纤溶酶降解纤维蛋白和纤维蛋白原。研究表明，将白色念珠菌加入固定化层黏连蛋白和纤连蛋白的微量滴定板，发现随着层黏连蛋白和纤连蛋白浓度的增高，黏附的细菌数量增多。在微量滴定板中加入GAPDH二抗，细菌黏附数量减少；当加入GAPDH时，随着GAPDH浓度的升高，抑制细菌黏附能力增强[41]。表明GAPDH能够与粘连蛋白和纤连蛋白结合，竞争性抑制细菌黏附。上文已提及，Glenting提取了乳酸杆菌*L. plantarum* strains 299v的表面蛋白，进行酶联免疫吸附反应，实验结果证实GAPDH能够与纤溶酶原、纤连蛋白和粘蛋白结合，但是GAPDH与粘蛋白结合的能力比与纤溶酶原和纤连蛋白结合的能力弱[18]。

4 细菌胞浆GAPDH向菌体表面分泌的机制

GAPDH原存在于细胞质内，随着研究深入，在细胞膜和细胞核内都发现GAPDH。化脓链球菌(*Streptococcus pyogenes*)表面的GAPDH也称为链球菌表面脱氢酶(Streptococcal surface dehydrogenase)，在培养的上清液中发现了与其它成分结合的可溶性GAPDH[42]。通常GAPDH紧密连接在化脓性链球菌的表面，用2 mol/L NaCl和2% SDS很难将细菌表面的GAPDH去除[28]。但是在模拟铁饥饿的培

养条件下，能促进化脓链球菌表面GAPDH释放到培养液[43]，促进GAPDH分泌到培养液的机制有待考证。研究发现，在肠致病性大肠杆菌中，GAPDH的分泌与囊泡无关，而是与生长条件有关。在三型ATP酶EscN缺陷的大肠杆菌中，GAPDH的分泌受到抑制，重组*escN*基因后，GAPDH分泌恢复。用覆盖免疫印记法和生物膜层反射光干涉技术发现，GAPDH与伴侣蛋白C密切相关，证实GAPDH的分泌与三型分泌系统(Type III secretion system，T3SS)有关[44]。目前，GAPDH如何转移到细胞外，GAPDH如何黏附到细胞膜上，这些机制都还有待进一步研究。

5 展望

GAPDH存在细胞核、细胞质和细胞膜上，位于细胞膜上的GAPDH参与细菌的黏附作用，包括有害菌黏附组织器官表面、侵袭宿主，益生菌定殖肠道、发挥益生作用。作者所在课题组通过提取不同黏附力乳酸杆菌的表面蛋白分析，发现高黏附力菌株的表面蛋白内含有GAPDH，将蛋白去除或用抗体封闭后，菌体对IPEC-J2和Caco-2细胞粘附能力下降，进一步证实益生菌GAPDH介导的肠道黏附作用。然而，GAPDH蛋白是如何锚定至微生物表面依然不清楚，目前研究认为GAPDH作为胞质酶不拥有任何信号肽或细胞锚定基序，甚至不含疏水膜生产区域，因此常被称为“无锚”蛋白。因此有人推测认为GAPDH蛋白经分泌至细菌表面时可能与细菌表面其他成分(如脂磷壁酸)存在电荷或者疏水性的互作。作者所在课题组通过I-TASSER等生物信息学软件在线预测GAPDH的粘附位点与跨膜结构，发现罗伊氏乳酸杆菌表面GAPDH蛋白有一段跨膜区域，可锚定至乳酸杆菌表面成分中，这有可能说明GAPDH蛋白可通过该序列稳定地连接至细胞表面上。这说明不同乳酸杆菌的GAPDH锚定在细菌表面方式可能不同。关于乳酸杆菌GAPDH如何分布，以及GAPDH如何转运并且黏附到细胞膜为课题组进一步深入研究方向。另一方面，明晰GAPDH介导的致病菌的黏附作用机制，调控减少致病菌对宿主的黏附，可预防、治疗动物肠道疾病，提高动物免疫力，促进动物健康。GAPDH参与多种疾病，如肿瘤、糖尿病和神经退行性疾病(阿尔兹海默症，帕金森病)的发生，对此开展研究，将为这些疾病的治疗提供了新方向。

参考文献

[1] Wang HF, Zhang WM, Wang YZ, Liu JX. Cell surface components of *Lactobacilli*: recent advances on their adherence mechanism of action in the gastroin testinal tract. *Acta Zoonutrimenta Sinica*, 2011, 23(2): 179–186. (in Chinese)
汪海峰, 章文明, 汪以真, 刘建新. 乳酸杆菌与肠道黏附相关表面因子及其机制的研究进展. 动物营养学报, 2011, 23(2): 179–186.

[2] Wu YH, Wu M, He GW, Zhang X, Li WG, Gao Y, Li ZH, Wang ZY, Zhang CG. Glyceraldehyde-3-phosphate dehydrogenase: a universal internal control for Western blots in prokaryotic and eukaryotic cells. *Analytical Biochemistry*, 2012, 423(1): 15–22.

[3] Tristan C, Shahani N, Sedlak TW, Sawa A. The diverse functions of GAPDH: views from different subcellular compartments. *Cellular Signalling*, 2011, 23(2): 317–323.

[4] Nelson DL, Cox MM. Lehninger Principles of Biochemistry. New York: Freeman, 2004.

[5] Singh R, Green MR. Sequence-specific binding of transfer RNA by glyceraldehyde-3-phosphate dehydrogenase. *Science*, 1993, 259(5093): 365–368.

[6] Zheng L, Roeder RG, Luo Y. S phase activation of the histone H2B promoter by OCA-S, a coactivator complex that contains GAPDH as a key component. *Cell*, 2003, 114(2): 255–266.

[7] Demple B, Harrison L. Repair of oxidative damage to DNA: enzymology and biology. *Annual Review of Biochemistry*, 1994, 63(1): 915–948.

[8] Demarse NA, Ponnusamy S, Spicer EK, Apohan E, Baatz JE, Ogretmen B, Davies C. Direct binding of glyceraldehyde 3-phosphate dehydrogenase to telomeric DNA protects telomeres

against chemotherapy-induced rapid degradation. *Journal of Molecular Biology*, 2009, 394(4): 789–803.

[9] Tisdale EJ. Glyceraldehyde-3-phosphate dehydrogenase is phosphorylated by protein kinase Cι/λ and plays a role in microtubule dynamics in the early secretory pathway. *The Journal of Biological Chemistry*, 2002, 277(5): 3334–3341.

[10] Engel M, Seifert M, Theisinger B, Seyfert U, Welter C. Glyceraldehyde-3-phosphate dehydrogenase and Nm23-H1/nucleoside diphosphate kinase A two old enzymes combine for the novel Nm23 protein phosphotransferase function. *The Journal of Biological Chemistry*, 1998, 273(32): 20058–20065.

[11] Kawamoto RM, Caswell AH. Autophosphorylation of glyceraldehyde phosphate dehydrogenase and phosphorylation of protein from skeletal muscle microsomes. *Biochemistry*, 1986, 25(3): 656–661.

[12] Sunaga K, Takahashi H, Chuang DM, Ishitani R. Glyceraldehyde-3-phosphate dehydrogenase is over-expressed during apoptotic death of neuronal cultures and is recognized by a monoclonal antibody against amyloid plaques from Alzheimer's brain. *Neuroscience Letters*, 1995, 200(2): 133–136.

[13] Kornberg MD, Sen N, Hara MR, Juluri KR, Nguyen JVK, Snowman AM, Law L, Hester LD, Snyder SH. GAPDH mediates nitrosylation of nuclear proteins. *Nature Cell Biology*, 2010, 12(11): 1094–1100.

[14] Sheokand N, Malhotra H, Kumar S, Tillu VA, Chauhan AS, Raje CI, Raje M. Moonlighting cell-surface GAPDH recruits apotransferrin to effect iron egress from mammalian cells. *Journal of Cell Science*, 2014, 127(19): 4279–4291.

[15] Liu S, Zhu PF, Zhang L, Li Z, Lv QJ, Zheng SJ, Wang Y, Lu FM. Increased glyceraldehyde-3-phosphate dehydrogenase expression indicates higher survival rates in male patients with hepatitis B virus-accociated hepatocellular carcinoma and cirrhosis. *Experimental and Therapeutic Medicine*, 2015, 9(5): 1597–1604.

[16] Hwang S, Disatnik MH, Mochly-Rosen D. Impaired GAPDH-induced mitophagy contributes to the pathology of Huntington's disease. *EMBO Molecular Medicine*, 2015, 7(10): 1307–1326.

[17] Liu L, Xiong N, Zhang P, Chen CN, Huang JS, Zhang GX, Xu XY, Shen Y, Lin ZC, Wang T. Genetic variants in GAPDH confer susceptibility to sporadic parkinson's disease in a Chinese han population. *PLoS One*, 2015, 10(8): e0135425.

[18] Glenting J, Beck HC, Vrang A, Riemann H, Ravn P, Hansen AM, Antonsson M, Ahrné S, Israelsen H, Madsen S. Anchorless surface associated glycolytic enzymes from *Lactobacillus plantarum* 299v bind to epithelial cells and extracellular matrix proteins. *Microbiological Research*, 2013, 168(5): 245–253.

[19] Zhang WM, Wang HF, Gao K, Wang C, Liu L, Liu JX. *Lactobacillus reuteri* glyceraldehyde-3-phosphate dehydrogenase functions in adhesion to intestinal epithelial cells. *Canadian Journal of Microbiology*, 2015, 61(5): 373–380.

[20] Ramiah K. Characterization of the adhesion genes of probiotic lactic acid bacteria, of Stellenbosch: Stellenbosch University, 2008.

[21] Spurbeck RR, Arvidson CG. *Lactobacillus jensenii* surface-associated proteins inhibit *Neisseria gonorrhoeae* adherence to epithelial cells. *Infection and Immunity*, 2010, 78(7): 3103–3111.

[22] Kinoshita H, Uchida H, Kawai Y, Kawasaki T, Wakahara N, Matsuo H, Watanabe M, Kitazawa H, Ohnuma S, Miura K, Horii A, Saito T. Cell surface *Lactobacillus plantarum* LA 318 glyceraldehyde-3-phosphate dehydrogenase (GAPDH) adheres to human colonic mucin. *Journal of Applied Microbiology*, 2008, 104(6): 1667–1674.

[23] Kinoshita H, Wakahara N, Watanabe M, Kawasaki T, Matsuo H, Kawai Y, Kitazawa H, Ohnuma S, Miura K, Horii A, Saito T. Cell surface glyceraldehyde-3-phosphate dehydrogenase (GAPDH) of *Lactobacillus plantarum* LA 318 recognizes human A and B blood group antigens. *Research in Microbiology*, 2008, 159(9/10): 685–691.

[24] Egea L, Aguilera L, Giménez R, Sorolla MA, Aguilar J, Badía J, Baldoma L. Role of secreted glyceraldehyde-3-phosphate dehydrogenase in the infection mechanism of enterohemorrhagic and enteropathogenic *Escherichia coli*: interaction of the extracellular enzyme with human plasminogen and fibrinogen. *The International Journal of Biochemistry & Cell Biology*, 2007, 39(6): 1190–1203.

[25] Tunio SA, Oldfield NJ, Ala'Aldeen DAA, Wooldridge KG, Turner DP. The role of glyceraldehyde 3-phosphate dehydrogenase (GapA-1) in *Neisseria meningitidis* adherence to human cells. *BMC Microbiology*, 2010, 10(1): 280.

[26] Gao K, Wang C, Liu L, Dou XX, Liu J, Yuan LJ, Zhang WM, Wang HF. Immunomodulation and signaling mechanism of *Lactobacillus rhamnosus* GG and its components on porcine

intestinal epithelial cells stimulated by lipopolysaccharide. *Journal of Microbiology*, *Immunology*, *and Infection*, 2015, doi: 10.1016/j.jmii.2015.05.002.

[27] Li PC, Yu QH, Ye XL, Wang ZS, Yang Q. *Lactobacillus* S-layer protein inhibition of *Salmonella*-induced reorganization of the cytoskeleton and activation of MAPK signalling pathways in Caco-2 cells. *Microbiology*, 2011, 157(Pt 9): 2639–2646.

[28] Pancholi V, Fischetti VA. A major surface protein on group A *Streptococci* is a glyceraldehyde-3-phosphate-dehydrogenase with multiple binding activity. *Journal of Experimental Medicine*, 1992, 176(2): 415–426.

[29] Matta SK, Agarwal S, Bhatnagar R. Surface localized and extracellular glyceraldehyde-3-phosphate dehydrogenase of *Bacillus anthracis* is a plasminogen binding protein. *Biochimica et Biophysica Acta*, 2010, 1804(11): 2111–2120.

[30] Alvarez-Dominguez C, Madrazo-Toca F, Fernandez-Prieto L, Vandekerckhove J, Pareja E, Tobes R, Gomez-Lopez MT, Del Cerro-Vadillo E, Fresno M, Leyva-Cobián F, Carrasco-Marín E. Characterization of a *Listeria monocytogenes* protein interfering with Rab5a. *Traffic*, 2008, 9(3): 325–337.

[31] Vedamurthy GV, Sahoo S, Devi IK, Murugavel S, Joshi P. The N-terminal segment of glyceraldehyde-3-phosphate dehydrogenase of *Haemonchus contortus* interacts with complements C1q and C3. *Parasite Immunology*, 2015, 37(11): 568–578.

[32] Jin H, Song YP, Boel G, Kochar J, Pancholi V. Group A *Streptococcal* surface GAPDH, SDH, recognizes uPAR/CD87 as its receptor on the human pharyngeal cell and mediates bacterial adherence to host cells. *Journal of Molecular Biology*, 2005, 350(1): 27–41.

[33] Seifert KN, McArthur WP, Bleiweis AS, Brady LJ. Characterization of group B *Streptococcal* glyceraldehyde-3-phosphate dehydrogenase: surface localization, enzymatic activity, and proteinprotein interactions. *Canadian Journal of Microbiology*, 2003, 49(5): 350–356.

[34] Quessy S, Busque P, Higgins R, Jacques M, Dubreuil JD. Description of an albumin binding activity for *Streptococcus suis* serotype 2. *FEMS Microbiology Letters*, 1997, 147(2): 245–250.

[35] Sánchez B, Schmitter JM, Urdaci MC. Identification of novel proteins secreted by *Lactobacillus plantarum* that bind to mucin and fibronectin. *Journal of Molecular Microbiology and Biotechnology*, 2009, 17(3): 158–162.

[36] Ramiah K, van Reenen CA, Dicks LMT. Surface-bound proteins of *Lactobacillus plantarum* 423 that contribute to adhesion of Caco-2 cells and their role in competitive exclusion and displacement of *Clostridium sporogenes* and *Enterococcus faecalis*. *Research in Microbiology*, 2008, 159(6): 470–475.

[37] Behera SK, Praharaj AB, Dehury B, Negi S. Exploring the role and diversity of mucins in health and disease with special insight into non-communicable diseases. *Glycoconjugate Journal*, 2015, 32(8): 575–613.

[38] Moncada DM, Kammanadiminti SJ, Chadee K. Mucin and toll-like receptors in host defense against intestinal parasites. *Trends in Parasitology*, 2003, 19(7): 305–311.

[39] Bhowmick R, Ghosal A, Das B, Koley H, Saha DR, Ganguly S, Nandy RK, Bhadra RK, Chatterjee NS. Intestinal adherence of *Vibrio* cholerae involves a coordinated interaction between colonization factor GbpA and mucin. *Infection and Immunity*, 2008, 76(11): 4968–4977.

[40] Beachey EH, Ofek I. Epithelial cell binding of group A *Streptococci* by lipoteichoic acid on fimbriae denuded of M protein. *Journal of Experimental Medicine*, 1976, 143(4): 759–771.

[41] Gozalbo D, Gil-Navarro I, Azorín I, Renau-Piqueras J, Martínez JP, Gil ML. The cell wall-associated glyceraldehyde-3-phosphate dehydrogenase of *Candida albicans* is also a fibronectin and laminin binding protein. *Infection and Immunity*, 1998, 66(5): 2052–2059.

[42] Terao Y, Yamaguchi M, Hamada S, Kawabata S. Multifunctional glyceraldehyde-3-phosphate dehydrogenase of *Streptococcus pyogenes* is essential for evasion from neutrophils. *The Journal of Biological Chemistry*, 2006, 281(20): 14215–14223.

[43] Eichenbaum Z, Green BD, Scott JR. Iron starvation causes release from the group A *Streptococcus* of the ADP-ribosylating protein called plasmin receptor or surface glyceraldehyde-3-phosphate-dehydrogenase. *Infection and Immunity*, 1996, 64(6): 1956–1960.

[44] Aguilera L, Ferreira E, Giménez R, Fernández FJ, Taulés M, Aguilar J, Vega MC, Badia J, Baldomà L. Secretion of the housekeeping protein glyceraldehyde-3-phosphate dehydrogenase by the LEE-encoded type Ⅲ secretion system in enteropathogenic *Escherichia coli*. *The International Journal of Biochemistry & Cell Biology*, 2012, 44(6): 955–962.

Mechanisms of glyceraldehyde 3-phosphosphate dehydrogenaseis in bacteria adhesion-A review

Li Liu, Wenming Zhang, Chong Wang, Haifeng Wang*

Institute of Animal Nutrition, College of Animal Science and Technology, Zhejiang A&F University, Lin'an 311300, Zhejiang Province, China

Abstract: Glyceraldehyde 3-phosphosphate dehydrogenaseis (GAPDH) acts as an enzymes of glycolysis and participates in the glycolytic pathway to generate energy. As a "housekeeping" protein, GAPDH is involved in many cellular processes in addition to glycolysis. These functions include DNA repair, tRNA export, facilitating microtubule polymerization, regulating the expression of the protein, and cell autophagy. Many researches indicated that bacterial surface GAPDH is involved in adhesion. This article reviews the basis function of GAPDH, and the role and mechanism of GAPDH in adhesion of bacteria.

Keywords: GAPDH, adherence, mechanism, bacteria

(本文责编：张晓丽)

Supported by the National Natural Science Foundation of China (31601951), by the Zhejiang Provincial Natural Science Foundation of China (Y14C170018) and by the China Spark Program (2015GA700001)

*Corresponding author. Tel/Fax: +86-571-63743313; E-mail: hfwang@zafu.edu.cn

Received: 22 November 2015; Revised: 25 February 2016; Published online: 29 Fabruary 2016