Traditional Chinese Medicine 中医学, 2025, 14(7), 3119-3129
Published Online July 2025 in Hans. https://www.hanspub.org/journal/tcm
https://doi.org/10.12677/tcm.2025.147460

Hans汉斯

葡萄糖代谢重编码调控Correa级联反应：中医防治胃癌的重要策略

龚玉霞[1*]，陈玉[2#]

[1]成都中医药大学临床医学院，四川 成都
[2]成都中医药大学附属医院肿瘤科，四川 成都

收稿日期：2025年5月31日；录用日期：2025年7月7日；发布日期：2025年7月21日

摘　要

胃癌是最常见的恶性肿瘤之一，Correa级联反应模式将胃癌的发展大致分为胃炎、胃癌前病变和胃癌三个阶段。在影响胃癌Correa级联反应发展的各类因素中，葡萄糖代谢重编码发挥着重要作用。本文总结了葡萄糖代谢重编码在胃癌Correa级联反应中的动态变化和分子机制，葡萄糖代谢重编码与自噬、上皮间充质转化、铁死亡和氧化应激通过相互串扰促进胃癌Correa级联反应。综上所述，中医在靶向葡萄糖代谢调控防治胃癌的Correa级联反应方面具有多靶点、多途径、疗效确切和副作用少的特点。

关键词

胃癌，Correa级联反应，葡萄糖代谢重编码，中医治疗

Glucose Metabolism Recoding Regulates the Correa Cascade Response: An Important Strategy for Gastric Cancer Prevention and Treatment in Traditional Chinese Medicine

Yuxia Gong[1*], Yu Chen[2#]

[1]School of Clinical Medicine, Chengdu University of Traditional Chinese Medicine, Chengdu Sichuan
[2]Department of Oncology, The First Affiliated Hospital of Heilongjiang University of Chinese Medicine, Chengdu Sichuan

Received: May 31st, 2025; accepted: Jul. 7th, 2025; published: Jul. 21st, 2025

*第一作者。
#通讯作者。

文章引用: 龚玉霞, 陈玉. 葡萄糖代谢重编码调控 Correa 级联反应: 中医防治胃癌的重要策略[J]. 中医学, 2025, 14(7): 3119-3129. DOI: 10.12677/tcm.2025.147460

Abstract

Gastric cancer is one of the most common malignant tumors, and the Correa cascade response model broadly classifies the development of gastric cancer into three stages: gastritis, gastric precancerous lesions and gastric cancer. Among the factors affecting the development of Correa cascade response in gastric cancer, glucose metabolic recoding plays an important role. In this paper, we summarize the dynamic changes and molecular mechanisms of glucose metabolic recoding in the Correa cascade response of gastric cancer, and glucose metabolic recoding and autophagy, epithelial mesenchymal transition, iron death and oxidative stress promote the Correa cascade response of gastric cancer through mutual crosstalk. It is concluded that TCM has the characteristics of multi-targets, multi-pathways, precise efficacy and few side effects in targeting glucose metabolism regulation to prevent and control Correa cascade response in gastric cancer.

Keywords

Gastric Cancer, Correa Cascade Response, Glucose Metabolism Recoding, Traditional Chinese Medicine Treatment

1. 引言

胃癌(Gastric cancer, GC)是常见的恶性肿瘤，由于其缺乏特异性的症状体征、检查方式相对单一等，导致被诊断为 GC 患者的五年生存率不足 38%，若能够早期诊治，患者的五年生存率可达到 77% [1]。根据 Lauren 分型[2]，肠型 GC 具有典型的 Correa 级联反应，即从正常胃粘膜组织微小粘膜病变发展为慢性非萎缩性胃炎(Chronic nonatrophic gastritis, NAG)、慢性萎缩性胃炎(Chronic atrophic gastritis, CAG)、肠化生和上皮瘤变/异型增生。因此，阻断或逆转 Correa 级联反应可能是防治 GC 的关键。糖代谢异常是多步骤致癌过程中的早期事件[3]，在各种慢性炎症的影响及糖代谢关键酶、转运蛋白、癌基因、信号通路的刺激下，正常胃粘膜组织可发生“损伤－修复－失代偿－异常增殖”的病理过程。在此期间，胃粘膜细胞糖代谢途径发生异常，促进肿瘤微环境形成，为细胞异常增殖提供原料和能量。这种糖代谢变化通过一种或多种机制发生，并与氧化应激、自噬、上皮间充质转化和铁死亡交互，促进 GC 发展。

2. 葡萄糖代谢促进 Correa 级联反应

2.1. 糖代谢与慢性胃炎

NAG 是以幽门螺杆菌(Helicobacter pylori, Hp)感染为主的多种病理因素引起的胃粘膜发生淋巴细胞、浆细胞浸润为主的病变。长期的炎症刺激使得胃粘膜充血水肿、皱襞肿胀增粗，NAG 患者胃粘膜受损导致细胞质 NAD/NADH 比率降低、葡萄糖和氧气消耗增加，氧化磷酸化增强[4]。当 Hp 急性感染损害胃粘膜时，葡萄糖-6 磷酸脱氢酶、苹果酸脱氢酶表达[5]，促进磷酸戊糖途径(Pentose phosphate pathway, PPP)、三羧酸循环(Tricarboxylic acid cycle, TAC)和无氧糖酵解[6]。代谢通量向 PPP 途径转移，产生高水平的谷胱甘肽[7]，增强清除活性氧能力，并激活 AMPK 信号通路，促进细胞自噬，使胃上皮细胞免受幽门螺杆菌诱导的细胞凋亡[8]，有利于胃黏膜的恢复。Hp 慢性感染时，糖代谢关键酶表达上调，导致 AMPK 失

活并刺激糖酵解、自噬的负向调节因子 BECN1、ATG12 [9]被激活，促进糖酵解、抑制自噬，抑制细胞修复，促进胃粘膜细胞和腺体的萎缩。

2.2. 葡萄糖代谢异常促进胃癌前病变的发生发展

随着慢性胃炎的反复发作，胃粘膜反复经历受损、修复，胃粘膜发生由正常上皮细胞向肠上皮化生、异型增生表型(又称上皮内瘤变或非浸润性肿瘤)的转变。在此阶段，TAC 进一步增强[10]，糖酵解已非常活跃，大量炎症因子[11]的产生及糖代谢关键酶的表达上调促进缺氧诱导因子 1-α (HIF-1α)、信号传导及转录激活蛋白 3 (Signal transduction and activation protein 3, STAT3)激活，诱导 p53 半衰期缩短。同时，NF-κB 作为关键信号通路被活性氧(Reactive oxygen species, ROS)、糖代谢酶激活，促进葡萄糖蛋白转运体 3 (Glucose protein transporter 3, GLUT3)表达，调节 TAC，激活 AKT/β-catenin 信号通路。PI3K/AKT 关键信号通路持续激活[12]，进一步促进糖代谢关键酶表达上调，并激活下游靶点 HIF-1α，促进胃组织、细胞葡萄糖代谢重编码，进一步诱导抑癌基因失活，促进胃癌前病变(Gastric precancerous lesions, GPL)向 GC 转变。

2.3. 胃癌阶段代谢重编码促进胃癌的发生发展

在胃癌阶段，糖酵解速率进一步增加，TAC 增强，琥珀酸盐代谢诱导炎症因子、炎症介质和 GLUT 表达上调[13]。丙酮酸激酶 2 (Pyruvate kinase 2, PKM2)作为上游靶点在 GC 阶段持续过表达，可诱导 HIF-1α 转录、与致癌基因相协调促进 AKT 磷酸化。HIF-1α 作为重要上游靶点，抑制丙酮酸的转化，并促进糖酵解靶基因的转录，诱导糖酵解酶和单羧酸盐转运蛋白 4 (Monocarboxylate transporter 4, MCT4)表达上调，共同作用介导乳酸通量，促进巨噬细胞 M2 样极化，促进 GC 细胞肿瘤微环境和葡萄糖代谢重编码。PI3K/AKT/mTOR 作为关键信号通路进一步激活，促进 p53 突变，解除其对糖酵解关键酶和蛋白[14]和下游靶基因[15]的抑制，诱导 Snail/FBP1、c-Myc 表达，提高 GC 细胞糖酵解速率，并参与自噬损伤，促进 GC 细胞上皮间充质转化(Epithelial-mesenchymal transition, EMT)。NF-κB 作为关键信号通路被激活，进一步激活 AKT/β-连环蛋白信号轴，促进致瘤细胞扩增，参与 GC 细胞的增殖、侵袭。

3. 糖代谢重编码与自噬、上皮细胞间充质转化、铁死亡和氧化应激相交互促进 Correa 级联反应

3.1. 糖酵解与自噬交互促进 Correa 级联反应

自噬即一个吞噬自身细胞质蛋白或细胞器并使其包被进入囊泡，与溶酶体融合形成自噬溶酶体，降解其所包裹的内容物，在响应细胞内应激、细胞稳态维持中起着关键作用[16]。爱泼斯坦－巴尔二氏病毒或 Hp 感染时会有效地激活自噬[17]，有利于细胞内病原体的快速清除。PI3K-AKT-mTOR 信号通路可调节细胞的凋亡、增殖和细胞自噬等[18]，并可通过能量产生活动(如 Warburg 效应)，维持 GC 的增殖需求[19]，自噬缺陷促进胃癌细胞糖酵解和转移[20]。在胃癌的 Correa 级联反应中，PI3K-AKT-mTOR 信号通路被解除控制，Hp 急性感染损害胃粘膜时，AMPK 信号通路激活[21]，抑制 mTORC1、磷酸化磷脂酰肌醇 3 激酶催化亚基 3，直接刺激自噬。Hp 慢性感染期间，肌肉丙酮酸激酶同工酶 2 (Pyruvate kinase isozyme typeM2, PKM2)过表达使得 AMPK 失活，抑制自噬[22]；PI3K/AKT 信号通路激活，进一步激活 mTORC1、Beclin-1 [23]表达上调，进一步抑制胃粘膜细胞自噬、诱导其糖酵解[24]。在 GPL 和 GC 阶段，PI3K-AKT-mTORC1 信号通路持续解除控制[25] [26]，并诱导糖酵解相关酶己糖激酶 2 (Hexokinase 2, HK2)、磷酸果糖激酶 2 (Fructose phosphate kinase 2, PFK2)、PKM2、乳酸脱氢酶 A (Lactate dehydrogenase A, LDHA)及 GLUT1 的表达[27]-[29]，增加葡萄糖摄取和糖酵解速率。PKM2 过表达促进 PI3K-AKT-mTORC1 激活以

抑制 GPL 和 GC 细胞的自噬[30]。在 GPL 阶段，胃粘膜中炎症水平较高，耗氧量增加，HIF-1α 表达上调，诱导 p53 突变。p53 作为抑癌基因，介导胃癌细胞的自噬并通过调节糖酵解关键酶和转运蛋白抑制糖酵解[31]。在 GC 阶段，PKM2 的过表达使得 p53 半衰期缩短、PI3K-AKT 通路激活，进一步诱导 mTOR、STAT3 表达，STAT3 作为 c-Myc 上游靶标[32]，被激活后诱导 c-Myc 表达。c-Myc 在 Corea 级联反应后期驱动多种糖酵解酶的表达以促进糖酵解[33]-[35]。

3.2. 葡萄糖代谢和上皮细胞间充质转化交互促进 Correa 级联反应

EMT 是指上皮细胞通过特定程序，转化为具有间质表型细胞的生物学过程，其特征是细胞黏附分子(如 E 钙黏蛋白)表达减少，角蛋白细胞骨架转化为波形蛋白为主的细胞骨架[36]。其活性影响肿瘤细胞的葡萄糖代谢重编程和侵袭性[37]。Hp 的毒力因子 γ-谷氨酰转移酶消耗胃中的谷氨酰胺，以减少 TAC 代谢物 α-酮戊二酸，激活 PI3K-AKT 信号通路[38]，促进间充质干细胞转移到胃中，并通过分化成上皮细胞或促进血管生成来参与 GC 的发展。Snail 家族基因是 EMT 的关键转录调节因子[37]，可调节葡萄糖通量并促进糖酵解和 PPP，使癌细胞在代谢应激下存活。Snail 在胃癌 Correa 级联反应中表达上调，Hp 感染时，ROS 介导的 Erk 活化和人胃癌细胞中糖原合成酶激酶 3β 通过 Ser9 位点的磷酸化而失活，进而诱导 Snail 表达并调节 EMT [39] [40]。果糖双磷酸酶 1 (Fructose bisphosphatase 1, FBP1)可逆转 Snail 诱导的胃癌细胞的糖酵解和 EMT [41]。Snail 的过表达增加了葡萄糖的利用率、乳酸聚集，抑制 FBP1 表达，促进 Correa 级联反应的糖酵解和 EMT。

果糖－二磷酸醛缩酶 A (Fructose-1,6-bisphosphate aldolase A, ALDOA)是主要存在于发育中的胚胎和成人肌肉中的裂解酶之一，参与糖的有氧氧化、无氧酵解和糖异生[42]，在 GC 中显著上调，并与胃癌预后相关[43]。在胃癌中，ALDOA 的表达与波形蛋白、N-钙粘蛋白、Snail 和锌指转录因子 1 呈正相关[44]，ALDOA 的表达可以增加 HIF-1α 的活性[44]，进一步调控 LDHA、ZEB2 的表达。随着乳酸聚集，ZEB2 可通过防止厌氧和有氧条件下乳酸的降解来提高 HIF-1α，促进胃癌细胞糖酵解和 EMT [45] [46]。PKM2 作为 HIF-1α 的靶向基因，促进 HIF-1 反式活化[47]，调控原癌基因 BCL-6 的表达，促进 E-钙粘蛋白的下调，波形蛋白和 N-钙粘蛋白表达上调[48]。6 磷酸果糖 2 激酶在胃癌细胞系中表达上调[49]，激活下游 Smad 蛋白、TGF-β，产生 EMT 允许状态，增强癌细胞中的 Snail 表达，诱导 NF-κB 上调，E-钙粘蛋白水平降低，N-钙粘蛋白和波形蛋白表达增加，促进 EMT [49] [50]和糖酵解。含有蛋白-1 的己糖激酶结构域在胃癌组织中上调[51]，通过增加葡萄糖消耗、乳酸的产生，触发 IkBa 降解来激活 NF-κB 信号传导[52]，同时上调锌指转录因子 1、N-钙粘蛋白、波形蛋白和 Snail 的水平，诱导胃癌细胞 EMT [51]。

3.3. 糖代谢重编码与铁死亡交互促进 Correa 级联反应

铁死亡是一种以铁依赖性脂质过氧化物死亡为主要特征的细胞程序性死亡方式，与癌症密切相关[53]。肿瘤细胞可以激活适应糖酵解、PPP 以满足肿瘤细胞对能量和生物合成日益增长的需求，维持氧化还原稳态以防止铁死亡。铁死亡与 GC 患者预后相关[54]。CAG 患者和大鼠在胃组织中表现出铁沉积，谷胱甘肽过氧化物酶 4 和铁蛋白重链 1 FTH 水平降低以及 4-羟基壬烯醛水平升高[55]，表明在 CAG 中存在铁死亡。PKM2 通过下调原癌基因 BCL-6 抑制铁死亡[56]。葡萄糖-6 磷酸脱氢酶促进 PPP，诱导 NADPH 合成增多，支持介导的胱氨酸摄入，并将其进一步转化为半胱氨酸用于谷胱甘肽合成，避免胃肿瘤细胞脂质活性氧的消除，从而抑制铁死亡[57] [58]。在 GPL 和 GC 阶段，PKM2、HK2、LDHA、血小板磷酸果糖激酶、葡萄糖-6 磷酸脱氢酶表达上调，PKM2、HK2 调节 Yes 相关蛋白[59]，糖酵解、PPP 增强，导致胃癌细胞铁死亡抗性增加。胃癌阶段，Wnt/β-catenin 信号转导通过靶向胃癌中的谷胱甘肽过氧化物酶 4 [60]，赋予铁死亡抗性。STAT3 在胃癌阶段被激活，促进 C-myc 转录，调控胃癌中铁死亡负调节特征基因抑制铁死亡[61]。

3.4. 葡萄糖代谢重编码和氧化应激交互促进 Correa 级联反应

氧化应激是 ROS 产生和天然抗氧化防御失衡的结果，使中性粒细胞炎性浸润，蛋白酶分泌增加，产生大量氧化中间产物。ROS 信号传导可以通过诱导 DNA 突变以及激活癌变促进肿瘤发生[62]。研究表明，胃癌组织氧化应激反应降低，氧化解毒能力减弱，诱导细胞死亡增加，促进 GC 发展[63]。去乙酰化酶 Sirtuin 3 (SIRT3)是 NAD+依赖性脱乙酰酶家族，具有调控细胞增殖、DNA 修复、线粒体能量稳态和抗氧化活性等多种生理功能[64]。SIRT3 与 LDHA 相互作用并脱乙酰化，增强 LDHA 活性，加速胃癌细胞糖酵解[65]。SIRT3 过表达可以使胃肠细胞中的 ROS 水平降低，激活锰超氧化物歧化酶，重新平衡细胞内 ROS 稳态，保护细胞免受氧化应激诱导损伤[65]。G6DP 是 PPP 中起着催化作用的酶，促进 NADPH 的合成[66]，合成核糖核苷酸和维持细胞内氧化还原稳态。在 G6DP 敲低的细胞中检测到 ROS 和 NADPH 氧化酶 2 活化增加和 AMPK 的激活，导致胃癌细胞中的 NADPH 降低，刺激氧化应激[67]，二者可以协调癌细胞代谢[67]。

4. 中医药靶向调控 Correa 级联反应的葡萄糖代谢重编码

在胃癌的 Correa 级联反应中，除了遗传和表观遗传学改变，还依赖于持续的能量供应，其中葡萄糖代谢重编码发挥了重要作用，其与自噬、EMT、铁死亡、氧化应激等相交互，促进胃癌肿瘤微环境形成、为胃癌的增殖提供能量、诱导肿瘤细胞的侵袭和转移[14]。在 NAG 时期，胃部的炎症或感染促进 PPP 和 AMPK 的激活，促进 ROS 的清除和启动自噬，促进胃黏膜细胞的修复[8]。在炎症介质介导 GC 的各类影响因素中，Hp 感染和炎症与非贲门胃癌发病密切相关[68]。长期使用非甾体抗炎药一定程度上能够有效减少 CAG 患者远期癌症发展[69]。因此，在 Correa 级联反应早期，可以通过根除 Hp 或使用抗炎药物以缓解炎症状态，减少炎症介质释放引起的葡萄糖代谢重编码。如雷贝拉唑通过靶向抑制胃上皮细胞 STAT3/HK2 抑制其糖酵解，改善 Hp 感染[70]；丁香提取物抑制 Hp 感染引起的 PI3K/AKT/mTOR 信号通路的解除、干扰 TAC [71]；小檗碱通过促进 TAC 介导的花生四烯酸代谢促进胃溃疡的愈合[72]；苍术提取物提高了抗炎因子相关的 IL-10、I kappa B α 的表达，抑制 NF-κB，显著改善胃组织的病理损伤[73]。

在 GPL 时期，炎性因子大量产生诱导糖代谢关键酶表达进一步上调、关键信号通路激活与抑癌基因的失活。GPL 是胃的炎癌转化的重要步骤，一旦达到该阶段，GC 的发生概率大大增加[74]。因此，在 GPL 时期及时进行葡萄糖代谢重编码的干预非常重要。除了内镜检查、根除 Hp、胃粘膜保护剂、抗氧化维生素等常规措施外，一些天然化合物及中医药对于 GPL 的靶向葡萄糖代谢重编码也展现出了潜在价值。如人参皂苷 3 抑制 TIGAR 的表达和 NADP 的产生，导致胃黏膜上皮中 ROS 浓度进一步升高，进而诱导胃黏膜上皮细胞凋亡[75]；黄芪甲苷 IV [76]通过靶向抑制 p53、HIF-1α、MCTs 和 LDHA 以阻断 GPL 的异常糖酵解；党参通过靶向抑制 LDH 和肌酸激酶表达，调控 GPL 的糖酵解和 TAC [77]；胃痞消抑制 PI3K/AKT/mTOR 和 HIF-1 信号通路激活[78]，四君子汤诱导胃粘膜细胞的氧化磷酸化抑制 GPL [79]，黄芪建中汤靶向调节 TAC、糖酵解抑制 GPL 代谢重编码[80] [81]；复方阿胶浆通过抑制 PI3K/AKT/HIF-1α 信号通路的过度激活调节能量代谢紊乱；小建中汤改善胃黏膜缺氧和调节 PI3K/AKT/mTOR 和 p53/AMPK/ULK1 信号通路来抑制 GPL 胃黏膜细胞的自噬和糖酵解[29]；乐胃饮加味方通过 PI3K/AKT/mTOR 信号通路调控糖酵解干预慢性萎缩性胃炎[82]。

在 GC 阶段，PI3K/AKT/mTOR 信号通路持续激活，诱导糖代谢关键酶、致癌基因激活及抑癌基因的失活，胃癌细胞葡萄糖代谢重编码进一步增强，并与抑制胃癌细胞自噬、促进 EMT 相互影响，为 GC 细胞的增殖、浸润、转移提供能量。抑制 PI3K/AKT/mTOR 激活已经证明可以导致肿瘤的消退[83]，有望成为治疗 GC 的新靶点。目前可通过葡萄糖类似物 FDG 的 PET 观察肿瘤葡萄糖代谢，预测癌症细胞代谢活性和抗癌治疗的反应[84]。目前，已有部分药物在 GC 患者中展现出良好的靶向抗葡萄糖代谢重编码的

作用，如 2-脱氧葡萄糖作为糖酵解抑制剂通过抑制糖酵解并阻止乳酸生成来抑制胃肿瘤细胞生长[85]，热解脱乙烯酮姜黄素 GO-Y022 与 2DG 合用对抑制糖酵解具有协同作用[86]，丹参酮 IIA [87]、人参皂苷 Rg3 可通过上调 miR-429 靶向抑制 PI3K/AKT/mTOR 信号通路以提高胃癌铂类化疗的敏感性，并减轻其耐药[88]。儿茶素抑制乳酸生成和 LDHA 活性[89]，干姜和黄连抑制 LDH、HIF1A、PKM 表达[90]，红景天提取物水景苷靶向抑制 PKM2、ENO1 和 GLUT1 [91]，甘草查尔酮 A 抑制 HK2、Akt、NF-κB 信号通路抑制胃癌细胞异常糖代谢和乳酸生成[92]。改良的健脾养正汤通过调控 PKM2/HIF-1α 信号转导，减少 PKM2 依赖性糖酵解来抑制 GC 细胞生长和 EMT [93]。

5. 小结

基于以上葡萄糖代谢重编码在 Correa 级联反应中的作用机制和分子特性：在胃癌发展的前期，应重视炎症对糖代谢主要途径的影响和作用，对于 Hp 感染或其他因素引起的胃炎患者，尽早根除 Hp 或进行积极的抗炎治疗，抑制炎症因子对糖代谢上游通路、关键靶点和自噬抑制因子的激活，减轻胃黏膜损伤。在 GPL 阶段，p53、糖代谢关键酶、PI3K/AKT、NF-κB 信号通路可作为抑制胃的炎癌转化的重要治疗靶点。在 GC 阶段，葡萄糖代谢进一步增强并与自噬、上皮间充质转化、铁死亡等交互，抑制 Wnt/β-catenin、PI3K/AKT、Snail/FBP1 信号通路和糖酵解关键酶表达是阻止胃癌发展的重要靶点。目前西医治疗主要通过改变饮食习惯、根除 Hp、胃粘膜保护剂、环氧合酶-2 抑制剂和内窥镜切除术或粘膜剥脱术等进行治疗[94]。这些干预措施对于降低 GC 的发生具有一定的积极意义，但其多局限于 Correa 级联反应的某一阶段，且效果存在争议[95]。而中医药在防治胃癌 Correa 级联反应的葡萄糖代谢重编码方面具有多靶点、多途径、多阶段、疗效确切且副作用少的特点，在防治胃癌的 Correa 级联反应中发挥了重要作用，为胃癌的防治提供了新思路。

参考文献

[1] Li, Y., Feng, A., Zheng, S., Chen, C. and Lyu, J. (2022) Recent Estimates and Predictions of 5-Year Survival in Patients with Gastric Cancer: A Model-Based Period Analysis. *Cancer Control*, **29**, 1-9. https://doi.org/10.1177/10732748221099227

[2] Laurén, P. (1965) The Two Histological Main Types of Gastric Carcinoma: Diffuse and So-Called Intestinal-Type Carcinoma. *Acta Pathologica Microbiologica Scandinavica*, **64**, 31-49. https://doi.org/10.1111/apm.1965.64.1.31

[3] Pavlova, N.N. and Thompson, C.B. (2016) The Emerging Hallmarks of Cancer Metabolism. *Cell Metabolism*, **23**, 27-47. https://doi.org/10.1016/j.cmet.2015.12.006

[4] Olguín-Martínez, M., Hernández-Espinosa, D.R. and Hernández-Muñoz, R. (2013) α-Tocopherol Administration Blocks Adaptive Changes in Cell NADH/NAD+ Redox State and Mitochondrial Function Leading to Inhibition of Gastric Mucosa Cell Proliferation in Rats. *Free Radical Biology and Medicine*, **65**, 1090-1100. https://doi.org/10.1016/j.freeradbiomed.2013.08.176

[5] Ortiz-Ramírez, P., Hernández-Ochoa, B., Ortega-Cuellar, D., González-Valdez, A., Martínez-Rosas, V., Morales-Luna, L., *et al*. (2022) Biochemical and Kinetic Characterization of the Glucose-6-Phosphate Dehydrogenase from *Helicobacter pylori* Strain 29CaP. *Microorganisms*, **10**, Article No. 1359. https://doi.org/10.3390/microorganisms10071359

[6] Liu, Y., Jin, Z., Qin, X. and Zheng, Q. (2020) Urinary Metabolomics Research for Huangqi Jianzhong Tang against Chronic Atrophic Gastritis Rats Based on 1H NMR and UPLC-Q/TOF Ms. *Journal of Pharmacy and Pharmacology*, **72**, 748-760. https://doi.org/10.1111/jphp.13242

[7] Patra, K.C. and Hay, N. (2014) The Pentose Phosphate Pathway and Cancer. *Trends in Biochemical Sciences*, **39**, 347-354. https://doi.org/10.1016/j.tibs.2014.06.005

[8] Lv, G., Zhu, H., Zhou, F., Lin, Z., Lin, G. and Li, C. (2014) Amp-Activated Protein Kinase Activation Protects Gastric Epithelial Cells from *Helicobacter pylori*-Induced Apoptosis. *Biochemical and Biophysical Research Communications*, **453**, 13-18. https://doi.org/10.1016/j.bbrc.2014.09.028

[9] Yang, M., Pi, H., Li, M., Xu, S., Zhang, L., Xie, J., *et al*. (2016) From the Cover: Autophagy Induction Contributes to Cadmium Toxicity in Mesenchymal Stem Cells via AMPK/FOXO3a/BECN1 Signaling. *Toxicological Sciences*, **154**, 101-114. https://doi.org/10.1093/toxsci/kfw144

[10] Kim, Y.L., Lee, W., Chung, S.H., Yu, B.M., Lee, Y.C. and Hong, J. (2022) Metabolic Alterations of Short-Chain Fatty Acids and TCA Cycle Intermediates in Human Plasma from Patients with Gastric Cancer. *Life Sciences*, **309**, Article ID: 121010. https://doi.org/10.1016/j.lfs.2022.121010

[11] Hong, J., Zuo, W., Wang, A. and Lu, N. (2016) *Helicobacter pylori* Infection Synergistic with IL-1β Gene Polymorphisms Potentially Contributes to the Carcinogenesis of Gastric Cancer. *International Journal of Medical Sciences*, **13**, 298-303. https://doi.org/10.7150/ijms.14239

[12] Zhang, S., Tian, W., Liu, Y., Ni, J., Zhang, D., Pan, H., *et al*. (2022) Mechanism of N-Methyl-N-Nitroso-Urea-Induced Gastric Precancerous Lesions in Mice. *Journal of Oncology*, **2022**, Article ID: 3780854. https://doi.org/10.1155/2022/3780854

[13] Tannahill, G.M., Curtis, A.M., Adamik, J., Palsson-McDermott, E.M., McGettrick, A.F., Goel, G., *et al*. (2013) Succinate Is an Inflammatory Signal That Induces IL-1β through HIF-1α. *Nature*, **496**, 238-242. https://doi.org/10.1038/nature11986

[14] Liu, Y., Zhang, Z., Wang, J., Chen, C., Tang, X., Zhu, J., *et al*. (2019) Metabolic Reprogramming Results in Abnormal Glycolysis in Gastric Cancer: A Review. *OncoTargets and Therapy*, **12**, 1195-1204. https://doi.org/10.2147/ott.s189687

[15] Jiang, L., Chen, Y., Min, G., Wang, J., Chen, W., Wang, H., *et al*. (2021) Bcl2-Associated Athanogene 4 Promotes the Invasion and Metastasis of Gastric Cancer Cells by Activating the PI3K/AKT/NF-κB/ZEB1 Axis. *Cancer Letters*, **520**, 409-421. https://doi.org/10.1016/j.canlet.2021.08.020

[16] Yim, W.W. and Mizushima, N. (2020) Lysosome Biology in Autophagy. *Cell Discovery*, **6**, Article No. 6. https://doi.org/10.1038/s41421-020-0141-7

[17] Zhang, L., Sung, J.J., Yu, J., Ng, S.C., Wong, S.H., Cho, C.H., *et al*. (2014) Xenophagy in *Helicobacter pylori*- and Epstein-Barr Virus-Induced Gastric Cancer. *The Journal of Pathology*, **233**, 103-112. https://doi.org/10.1002/path.4351

[18] Huang, Q., Ou, Y., Tao, Y., Yin, H. and Tu, P. (2016) Apoptosis and Autophagy Induced by Pyropheophorbide-*A* Methyl Ester-Mediated Photodynamic Therapy in Human Osteosarcoma MG-63 Cells. *Apoptosis*, **21**, 749-760. https://doi.org/10.1007/s10495-016-1243-4

[19] Giguère, V. (2018) Canonical Signaling and Nuclear Activity of mTOR—A Teamwork Effort to Regulate Metabolism and Cell Growth. *The FEBS Journal*, **285**, 1572-1588. https://doi.org/10.1111/febs.14384

[20] Qin, W., Li, C., Zheng, W., Guo, Q., Zhang, Y., Kang, M., *et al*. (2015) Inhibition of Autophagy Promotes Metastasis and Glycolysis by Inducing ROS in Gastric Cancer Cells. *Oncotarget*, **6**, 39839-39854. https://doi.org/10.18632/oncotarget.5674

[21] Zhao, H., Zhu, H., Lin, Z., Lin, G. and Lv, G. (2015) Compound 13, an *A*1-Selective Small Molecule Activator of AMPK, Inhibits *Helicobacter pylori*-Induced Oxidative Stresses and Gastric Epithelial Cell Apoptosis. *Biochemical and Biophysical Research Communications*, **463**, 510-517. https://doi.org/10.1016/j.bbrc.2015.05.059

[22] Zhang, F., Chen, C., Hu, J., Su, R., Zhang, J., Han, Z., *et al*. (2019) Molecular Mechanism of *Helicobacter pylori*-Induced Autophagy in Gastric Cancer (Review). *Oncology Letters*, **18**, 6221-6227. https://doi.org/10.3892/ol.2019.10976

[23] Ahn, C.H., Jeong, E.G., Lee, J.W., Kim, M.S., Kim, S.H., Kim, S.S., *et al*. (2007) Expression of Beclin-1, an Autophagy-Related Protein, in Gastric and Colorectal Cancers. *APMIS*, **115**, 1344-1349. https://doi.org/10.1111/j.1600-0463.2007.00858.x

[24] He, C., Bian, Y., Xue, Y., Liu, Z., Zhou, K., Yao, C., *et al*. (2016) Pyruvate Kinase M2 Activates mTORC1 by Phosphorylating AKT1S1. *Scientific Reports*, **6**, Article No. 21524. https://doi.org/10.1038/srep21524

[25] Fattahi, S., Amjadi-Moheb, F., Tabaripour, R., Ashrafi, G.H. and Akhavan-Niaki, H. (2020) PI3K/AKT/mTOR Signaling in Gastric Cancer: Epigenetics and Beyond. *Life Sciences*, **262**, Article ID: 118513. https://doi.org/10.1016/j.lfs.2020.118513

[26] Zhu, F., Xu, Y., Pan, J., Li, M., Chen, F. and Xie, G. (2021) Epigallocatechin Gallate Protects against MNNG-Induced Precancerous Lesions of Gastric Carcinoma in Rats via PI3K/AKT/mTOR Pathway. *Evidence-Based Complementary and Alternative Medicine*, **2021**, Article ID: 8846813. https://doi.org/10.1155/2021/8846813

[27] Wang, Y., Zhou, Y., Xie, J., Zhang, X., Wang, S., Li, Q., *et al*. (2023) MAOA Suppresses the Growth of Gastric Cancer by Interacting with NDRG1 and Regulating the Warburg Effect through the PI3K/AKT/mTOR Pathway. *Cellular Oncology*, **46**, 1429-1444. https://doi.org/10.1007/s13402-023-00821-w

[28] Wu, J., Yuan, M., Shen, J., Chen, Y., Zhang, R., Chen, X., *et al*. (2022) Effect of Modified Jianpi Yangzheng on Regulating Content of PKM2 in Gastric Cancer Cells-Derived Exosomes. *Phytomedicine*, **103**, Article ID: 154229. https://doi.org/10.1016/j.phymed.2022.154229

[29] Zhang, J., Bao, S., Chen, J., Chen, T., Wei, H., Zhou, X., *et al*. (2023) Xiaojianzhong Decoction Prevents Gastric Precancerous Lesions in Rats by Inhibiting Autophagy and Glycolysis in Gastric Mucosal Cells. *World Journal of Gastrointestinal Oncology*, **15**, 464-489. https://doi.org/10.4251/wjgo.v15.i3.464

[30] Wang, C., Jiang, J., Ji, J., Cai, Q., Chen, X., Yu, Y., *et al*. (2017) PKM2 Promotes Cell Migration and Inhibits Autophagy

by Mediating PI3K/AKT Activation and Contributes to the Malignant Development of Gastric Cancer. *Scientific Reports*, **7**, Article No. 2886. https://doi.org/10.1038/s41598-017-03031-1

[31] Cao, Y., Luo, Y., Zou, J., Ouyang, J., Cai, Z., Zeng, X., *et al*. (2019) Autophagy and Its Role in Gastric Cancer. *Clinica Chimica Acta*, **489**, 10-20. https://doi.org/10.1016/j.cca.2018.11.028

[32] Yun, S., Yun, C.W., Lee, J.H., Kim, S. and Lee, S.H. (2017) Cripto Enhances Proliferation and Survival of Mesenchymal Stem Cells by Up-Regulating JAK2/STAT3 Pathway in a GRP78-Dependent Manner. *Biomolecules & Therapeutics*, **26**, 464-473. https://doi.org/10.4062/biomolther.2017.099

[33] Düvel, K., Yecies, J.L., Menon, S., Raman, P., Lipovsky, A.I., Souza, A.L., *et al*. (2010) Activation of a Metabolic Gene Regulatory Network Downstream of mTOR Complex 1. *Molecular Cell*, **39**, 171-183. https://doi.org/10.1016/j.molcel.2010.06.022

[34] Gao, S., Chen, M., Wei, W., Zhang, X., Zhang, M., Yao, Y., *et al*. (2018) Crosstalk of mTOR/PKM2 and STAT3/c-Myc Signaling Pathways Regulate the Energy Metabolism and Acidic Microenvironment of Gastric Cancer. *Journal of Cellular Biochemistry*, **120**, 1193-1202. https://doi.org/10.1002/jcb.26915

[35] Mossmann, D., Park, S. and Hall, M.N. (2018) mTOR Signalling and Cellular Metabolism Are Mutual Determinants in Cancer. *Nature Reviews Cancer*, **18**, 744-757. https://doi.org/10.1038/s41568-018-0074-8

[36] Nieto, M.A., Huang, R.Y., Jackson, R.A. and Thiery, J.P. (2016) EMT: 2016. *Cell*, **166**, 21-45. https://doi.org/10.1016/j.cell.2016.06.028

[37] Sung, J. and Cheong, J. (2021) Pan-Cancer Analysis Reveals Distinct Metabolic Reprogramming in Different Epithelial-mesenchymal Transition Activity States. *Cancers*, **13**, Article No. 1778. https://doi.org/10.3390/cancers13081778

[38] Wang, Z., Wang, W., Shi, H., Meng, L., Jiang, X., Pang, S., *et al*. (2022) Gamma-Glutamyltransferase of *Helicobacter pylori* Alters the Proliferation, Migration, and Pluripotency of Mesenchymal Stem Cells by Affecting Metabolism and Methylation Status. *Journal of Microbiology*, **60**, 627-639. https://doi.org/10.1007/s12275-022-1575-4

[39] Ngo, H., Lee, H.G., Piao, J., Zhong, X., Lee, H., Han, H., *et al*. (2016) *Helicobacter pylori* Induces Snail Expression through Ros-Mediated Activation of Erk and Inactivation of GSK-3β in Human Gastric Cancer Cells. *Molecular Carcinogenesis*, **55**, 2236-2246. https://doi.org/10.1002/mc.22464

[40] Zhou, B.P., Deng, J., Xia, W., Xu, J., Li, Y.M., Gunduz, M., *et al*. (2004) Dual Regulation of Snail by GSK-3β-Mediated Phosphorylation in Control of Epithelial-Mesenchymal Transition. *Nature Cell Biology*, **6**, 931-940. https://doi.org/10.1038/ncb1173

[41] Li, J., Wang, Y., Li, Q., Xue, J., Wang, Z., Yuan, X., *et al*. (2016) Downregulation of FBP1 Promotes Tumor Metastasis and Indicates Poor Prognosis in Gastric Cancer via Regulating Epithelial-Mesenchymal Transition. *PLOS ONE*, **11**, e0167857. https://doi.org/10.1371/journal.pone.0167857

[42] Ji, S., Zhang, B., Liu, J., Qin, Y., Liang, C., Shi, S., *et al*. (2016) ALDOA Functions as an Oncogene in the Highly Metastatic Pancreatic Cancer. *Cancer Letters*, **374**, 127-135. https://doi.org/10.1016/j.canlet.2016.01.054

[43] Chen, L., Wu, Z., Guo, J., Wang, X., Zhao, Z., Liang, H., *et al*. (2022) Initial Clinical and Experimental Analyses of ALDOA in Gastric Cancer, as a Novel Prognostic Biomarker and Potential Therapeutic Target. *Clinical and Experimental Medicine*, **23**, 2443-2456. https://doi.org/10.1007/s10238-022-00952-8

[44] Jiang, Z., Wang, X., Li, J., Yang, H. and Lin, X. (2018) Aldolase a as a Prognostic Factor and Mediator of Progression via Inducing Epithelial-Mesenchymal Transition in Gastric Cancer. *Journal of Cellular and Molecular Medicine*, **22**, 4377-4386. https://doi.org/10.1111/jcmm.13732

[45] Dai, Y., Tang, Y., Zhu, H., Lv, L., Chu, Y., Zhou, Y., *et al*. (2012) ZEB2 Promotes the Metastasis of Gastric Cancer and Modulates Epithelial Mesenchymal Transition of Gastric Cancer Cells. *Digestive Diseases and Sciences*, **57**, 1253-1260. https://doi.org/10.1007/s10620-012-2042-6

[46] Zhang, Y., Lin, S., Chen, Y., Yang, F. and Liu, S. (2018) LDH-A Promotes Epithelial-Mesenchymal Transition by Upregulating ZEB2 in Intestinal-Type Gastric Cancer. *OncoTargets and Therapy*, **11**, 2363-2373. https://doi.org/10.2147/ott.s163570

[47] de Wit, R.H., Mujić-Delić, A., van Senten, J.R., Fraile-Ramos, A., Siderius, M. and Smit, M.J. (2016) Human Cytomegalovirus Encoded Chemokine Receptor US28 Activates the HIF-1α/PKM2 Axis in Glioblastoma Cells. *Oncotarget*, **7**, 67966-67985. https://doi.org/10.18632/oncotarget.11817

[48] Li, N., Meng, D., Xu, Y., Gao, L., Shen, F., Tie, X., *et al*. (2020) Pyruvate Kinase M2 Knockdown Suppresses Migration, Invasion, and Epithelial-Mesenchymal Transition of Gastric Carcinoma via Hypoxia-Inducible Factor Alpha/B-Cell Lymphoma 6 Pathway. *BioMed Research International*, **2020**, Article ID: 7467104. https://doi.org/10.1155/2020/7467104

[49] Lei, L., Hong, L., Ling, Z., Zhong, Y., Hu, X., Li, P., *et al*. (2021) A Potential Oncogenic Role for PFKFB3 Overexpression in Gastric Cancer Progression. *Clinical and Translational Gastroenterology*, **12**, e00377. https://doi.org/10.14309/ctg.0000000000000377

[50] He, X., Cheng, X., Ding, J., Xiong, M., Chen, B. and Cao, G. (2022) Hyperglycemia Induces miR-26-5p Down-Regulation to Overexpress PFKFB3 and Accelerate Epithelial-Mesenchymal Transition in Gastric Cancer. *Bioengineered*, **13**, 2902-2917. https://doi.org/10.1080/21655979.2022.2026730

[51] Wang, M., Chen, Y., Xu, H., Zhan, J., Suo, D., Wang, J., *et al*. (2023) HKDC1 Upregulation Promotes Glycolysis and Disease Progression, and Confers Chemoresistance onto Gastric Cancer. *Cancer Science*, **114**, 1365-1377. https://doi.org/10.1111/cas.15692

[52] Zhao, J., Tian, M., Zhang, S., Delfarah, A., Gao, R., Rao, Y., *et al*. (2020) Deamidation Shunts Rela from Mediating Inflammation to Aerobic Glycolysis. *Cell Metabolism*, **31**, 937-955.e7. https://doi.org/10.1016/j.cmet.2020.04.006

[53] Jiang, X., Stockwell, B.R. and Conrad, M. (2021) Ferroptosis: Mechanisms, Biology and Role in Disease. *Nature Reviews Molecular Cell Biology*, **22**, 266-282. https://doi.org/10.1038/s41580-020-00324-8

[54] Chen, X., Zhu, Z., Li, X., Yao, X. and Luo, L. (2021) The Ferroptosis-Related Noncoding RNA Signature as a Novel Prognostic Biomarker in the Tumor Microenvironment, Immunotherapy, and Drug Screening of Gastric Adenocarcinoma. *Frontiers in Oncology*, **11**, Article 778557. https://doi.org/10.3389/fonc.2021.778557

[55] Zhao, Y., Zhao, J., Ma, H., Han, Y., Xu, W., Wang, J., *et al*. (2023) High Hepcidin Levels Promote Abnormal Iron Metabolism and Ferroptosis in Chronic Atrophic Gastritis. *Biomedicines*, **11**, Article No. 2338. https://doi.org/10.3390/biomedicines11092338

[56] Guo, S., Deng, J., Wang, P., Kou, F., Wu, Z., Zhang, N., *et al*. (2023) The Malignancy Suppression and Ferroptosis Facilitation of BCL6 in Gastric Cancer Mediated by FZD7 Repression Are Strengthened by RNF180/RhoC Pathway. *Cell & Bioscience*, **13**, Article No. 73. https://doi.org/10.1186/s13578-023-01020-8

[57] Liu, X., Olszewski, K., Zhang, Y., Lim, E.W., Shi, J., Zhang, X., *et al*. (2020) Cystine Transporter Regulation of Pentose Phosphate Pathway Dependency and Disulfide Stress Exposes a Targetable Metabolic Vulnerability in Cancer. *Nature Cell Biology*, **22**, 476-486. https://doi.org/10.1038/s41556-020-0496-x

[58] Seco-Cervera, M., González-Cabo, P., Pallardó, F., Romá-Mateo, C. and García-Giménez, J. (2020) Thioredoxin and Glutaredoxin Systems as Potential Targets for the Development of New Treatments in Friedreich's Ataxia. *Antioxidants*, **9**, Article No. 1257. https://doi.org/10.3390/antiox9121257

[59] Deng, H., Jia, Q., Ming, X., Sun, Y., Lu, Y., Liu, L., *et al*. (2023) Hippo Pathway in Intestinal Diseases: Focusing on Ferroptosis. *Frontiers in Cell and Developmental Biology*, **11**, Article 1291686. https://doi.org/10.3389/fcell.2023.1291686

[60] Wang, Y., Zheng, L., Shang, W., Yang, Z., Li, T., Liu, F., *et al*. (2022) Wnt/Beta-Catenin Signaling Confers Ferroptosis Resistance by Targeting GPX4 in Gastric Cancer. *Cell Death & Differentiation*, **29**, 2190-2202. https://doi.org/10.1038/s41418-022-01008-w

[61] Ouyang, S., Li, H., Lou, L., Huang, Q., Zhang, Z., Mo, J., *et al*. (2022) Inhibition of STAT3-Ferroptosis Negative Regulatory Axis Suppresses Tumor Growth and Alleviates Chemoresistance in Gastric Cancer. *Redox Biology*, **52**, Article ID: 102317. https://doi.org/10.1016/j.redox.2022.102317

[62] Gorrini, C., Harris, I.S. and Mak, T.W. (2013) Modulation of Oxidative Stress as an Anticancer Strategy. *Nature Reviews Drug Discovery*, **12**, 931-947. https://doi.org/10.1038/nrd4002

[63] Liu, Y., Shi, Y., Han, R., Liu, C., Qin, X., Li, P., *et al*. (2023) Signaling Pathways of Oxidative Stress Response: The Potential Therapeutic Targets in Gastric Cancer. *Frontiers in Immunology*, **14**, Article 1139589. https://doi.org/10.3389/fimmu.2023.1139589

[64] Ansari, A., Rahman, M.S., Saha, S.K., Saikot, F.K., Deep, A. and Kim, K. (2016) Function of the SIRT3 Mitochondrial Deacetylase in Cellular Physiology, Cancer, and Neurodegenerative Disease. *Aging Cell*, **16**, 4-16. https://doi.org/10.1111/acel.12538

[65] Cui, Y., Qin, L., Wu, J., Qu, X., Hou, C., Sun, W., *et al*. (2015) SIRT3 Enhances Glycolysis and Proliferation in SIRT3-Expressing Gastric Cancer Cells. *PLOS ONE*, **10**, e0129834. https://doi.org/10.1371/journal.pone.0129834

[66] Morales-Luna, L., Hernández-Ochoa, B., Martínez-Rosas, V., González-Valdez, A., Cárdenas-Rodríguez, N., Enríquez-Flores, S., *et al*. (2021) Cloning, Purification, and Characterization of the 6-Phosphogluconate Dehydrogenase (6 PGDH) from Giardia Lamblia. *Molecular and Biochemical Parasitology*, **244**, Article ID: 111383. https://doi.org/10.1016/j.molbiopara.2021.111383

[67] Chen, C., Du, P., Zhang, Z. and Bao, D. (2023) 6-Phosphogluconate Dehydrogenase Inhibition Arrests Growth and Induces Apoptosis in Gastric Cancer via AMPK Activation and Oxidative Stress. *Open Life Sciences*, **18**, Article ID: 20220514. https://doi.org/10.1515/biol-2022-0514

[68] Collatuzzo, G., Pelucchi, C., Negri, E., López-Carrillo, L., Tsugane, S., Hidaka, A., *et al*. (2021) Exploring the Interactions between *Helicobacter pylori* (Hp) Infection and Other Risk Factors of Gastric Cancer: A Pooled Analysis in the Stomach Cancer Pooling (StoP) Project. *International Journal of Cancer*, **149**, 1228-1238. https://doi.org/10.1002/ijc.33678

[69] Yanaoka, K., Oka, M., Yoshimura, N., Deguchi, H., Mukoubayashi, C., Enomoto, S., *et al*. (2009) Preventive Effects of Etodolac, a Selective Cyclooxygenase-2 Inhibitor, on Cancer Development in Extensive Metaplastic Gastritis, a *Helicobacter*

pylori-Negative Precancerous Lesion. *International Journal of Cancer*, **126**, 1467-1473. https://doi.org/10.1002/ijc.24862

[70] Zhou, Y., Chen, S., Yang, F., Zhang, Y., Xiong, L., Zhao, J., *et al*. (2021) Rabeprazole Suppresses Cell Proliferation in Gastric Epithelial Cells by Targeting Stat3-Mediated Glycolysis. *Biochemical Pharmacology*, **188**, Article ID: 114525. https://doi.org/10.1016/j.bcp.2021.114525

[71] Peng, C., Sang, S., Shen, X., Zhang, W., Yan, J., Chen, P., *et al*. (2022) *In Vitro* Anti-*Helicobacter pylori* Activity of *Syzygium aromaticum* and the Preliminary Mechanism of Action. *Journal of Ethnopharmacology*, **288**, Article ID: 114995. https://doi.org/10.1016/j.jep.2022.114995

[72] Guo, Q., Lu, T., Zhang, M., Wang, Q., Zhao, M., Wang, T., *et al*. (2024) Protective Effect of Berberine on Acute Gastric Ulcer by Promotion of Tricarboxylic Acid Cycle-Mediated Arachidonic Acid Metabolism. *Journal of Inflammation Research*, **17**, 15-28. https://doi.org/10.2147/jir.s436653

[73] Zhen, B., Cai, Q. and Li, F. (2023) Chemical Components and Protective Effects of *Atractylodes japonica* Koidz. ex Kitam against Acetic Acid-Induced Gastric Ulcer in Rats. *World Journal of Gastroenterology*, **29**, 5848-5864. https://doi.org/10.3748/wjg.v29.i43.5848

[74] Piazuelo, M.B., Bravo, L.E., Mera, R.M., Camargo, M.C., Bravo, J.C., Delgado, A.G., *et al*. (2021) The Colombian Chemoprevention Trial: 20-Year Follow-Up of a Cohort of Patients with Gastric Precancerous Lesions. *Gastroenterology*, **160**, 1106-1117.e3. https://doi.org/10.1053/j.gastro.2020.11.017

[75] Liu, W., Pan, H., Yang, L., Zhao, Z., Yuan, D., Liu, Y., *et al*. (2020) *Panax ginseng* C.A. Meyer (Rg3) Ameliorates Gastric Precancerous Lesions in Atp4a$^{-/-}$ Mice via Inhibition of Glycolysis through PI3K/AKT/miRNA-21 Pathway. *Evidence-Based Complementary and Alternative Medicine*, **2020**, Article ID: 2672648. https://doi.org/10.1155/2020/2672648

[76] Yang, L., Li, J., Hu, Z., Fan, X., Cai, T., *et al*. (2020) A Systematic Review of the Mechanisms Underlying Treatment of Gastric Precancerous Lesions by Traditional Chinese Medicine. *Evidence-Based Complementary and Alternative Medicine*, **2020**, Article ID: 9154738. https://doi.org/10.1155/2020/9154738

[77] He, R., Ma, R., Jin, Z., Zhu, Y., Yang, F., Hu, F., *et al*. (2022) Proteomics and Metabolomics Unveil *Codonopsis pilosula* (Franch.) Nannf. Ameliorates Gastric Precancerous Lesions via Regulating Energy Metabolism. *Frontiers in Pharmacology*, **13**, Article 933096. https://doi.org/10.3389/fphar.2022.933096

[78] Cai, T., Zhang, C., Zeng, X., Zhao, Z., Yan, Y., Yu, X., *et al*. (2019) Protective Effects of Weipixiao Decoction against MNNG-Induced Gastric Precancerous Lesions in Rats. *Biomedicine & Pharmacotherapy*, **120**, Article ID: 109427. https://doi.org/10.1016/j.biopha.2019.109427

[79] Zhu, Y., Ma, R., Cheng, W., Qin, M., Guo, W., Qi, Y., *et al*. (2024) Sijunzi Decoction Ameliorates Gastric Precancerous Lesions via Regulating Oxidative Phosphorylation Based on Proteomics and Metabolomics. *Journal of Ethnopharmacology*, **318**, Article ID: 116925. https://doi.org/10.1016/j.jep.2023.116925

[80] Li, X., Li, A., Li, K., Qin, X. and Liu, Y. (2020) Metabonomics Approach Reveals the Vital Role of Huangqi in Huangqi Jianzhong Tang against Chronic Atrophic Gastritis Coupled with Molecular Docking and BAWP. *Chemometrics and Intelligent Laboratory Systems*, **200**, Article ID: 103984. https://doi.org/10.1016/j.chemolab.2020.103984

[81] Liu, Y., Xu, W., Wang, G. and Qin, X. (2018) Material Basis Research for Huangqi Jianzhong Tang against Chronic Atrophic Gastritis Rats through Integration of Urinary Metabonomics and Systemsdock. *Journal of Ethnopharmacology*, **223**, 1-9. https://doi.org/10.1016/j.jep.2018.05.015

[82] 叶芸, 李春灵, 等. 乐胃饮加味方通过PI3K/AKT/mTOR信号通路调控糖酵解干预慢性萎缩性胃炎[J]. 中国中西医结合杂志, 2025, 45(2): 190-197.

[83] Alzahrani, A.S. (2019) PI3K/AKT/mTOR Inhibitors in Cancer: At the Bench and Bedside. *Seminars in Cancer Biology*, **59**, 125-132. https://doi.org/10.1016/j.semcancer.2019.07.009

[84] Tixier, F., Hatt, M., Le Rest, C.C., Le Pogam, A., Corcos, L. and Visvikis, D. (2012) Reproducibility of Tumor Uptake Heterogeneity Characterization through Textural Feature Analysis in ^{18}F-FDG PET. *Journal of Nuclear Medicine*, **53**, 693-700. https://doi.org/10.2967/jnumed.111.099127

[85] Takizawa, K., Muramatsu, K., Maruyama, K., Urakami, K., Sugino, T., Kusuhara, M., *et al*. (2020) Metabolic Profiling of Human Gastric Cancer Cells Treated with Salazosulfapyridine. *Technology in Cancer Research & Treatment*, **19**, 1-12. https://doi.org/10.1177/1533033820928621

[86] MaruYama, T., Miyazaki, H., Lim, Y., Gu, J., Ishikawa, M., Yoshida, T., *et al*. (2023) Pyrolyzed Deketene Curcumin Controls Regulatory T Cell Generation and Gastric Cancer Metabolism Cooperate with 2-Deoxy-d-glucose. *Frontiers in Immunology*, **14**, Article 1049713. https://doi.org/10.3389/fimmu.2023.1049713

[87] Guan, Z., Chen, J., Li, X. and Dong, N. (2020) Tanshinone IIA Induces Ferroptosis in Gastric Cancer Cells through p53-Mediated SLC7A11 Down-Regulation. *Bioscience Reports*, **40**, BSR20201807. https://doi.org/10.1042/bsr20201807

[88] Wang, X., He, R., Geng, L., Yuan, J. and Fan, H. (2022) Ginsenoside Rg3 Alleviates Cisplatin Resistance of Gastric Cancer

Cells through Inhibiting SOX2 and the PI3K/AKT/mTOR Signaling Axis by Up-Regulating miR-429. *Frontiers in Genetics*, **13**, Article 823182. https://doi.org/10.3389/fgene.2022.823182

[89] Tao, H., Ding, X., Wu, J., Liu, S., Sun, W., Nie, M., *et al*. (2020) *β*-Asarone Increases Chemosensitivity by Inhibiting Tumor Glycolysis in Gastric Cancer. *Evidence-Based Complementary and Alternative Medicine*, **2020**, Article ID: 6981520. https://doi.org/10.1155/2020/6981520

[90] 傅敏. 黄连-干姜药对化学成分分析及其抗胃癌药效作用研究[D]: [硕士学位论文]. 武汉: 湖北中医药大学, 2022.

[91] Dai, Z., Zhang, X., Li, W., Tang, J., Pan, T., Ma, C., *et al*. (2021) Salidroside Induces Apoptosis in Human Gastric Cancer Cells *via* the Downregulation of ENO1/PKM2/GLUT1 Expression. *Biological and Pharmaceutical Bulletin*, **44**, 1724-1731. https://doi.org/10.1248/bpb.b21-00443

[92] Wu, J., Zhang, X., Wang, Y., Sun, Q., Chen, M., Liu, S., *et al*. (2017) Licochalcone A Suppresses Hexokinase 2-Mediated Tumor Glycolysis in Gastric Cancer via Downregulation of the Akt Signaling Pathway. *Oncology Reports*, **39**, 1181-1190. https://doi.org/10.3892/or.2017.6155

[93] Sun, Q., Yuan, M., Wang, H., Zhang, X., Zhang, R., Wang, H., *et al*. (2021) PKM2 Is the Target of a Multi-Herb-Combined Decoction during the Inhibition of Gastric Cancer Progression. *Frontiers in Oncology*, **11**, Article 767116. https://doi.org/10.3389/fonc.2021.767116

[94] Cao, Y., Wang, D., Mo, G., Peng, Y. and Li, Z. (2023) Gastric Precancerous Lesions: Occurrence, Development Factors, and Treatment. *Frontiers in Oncology*, **13**, Article 1226652. https://doi.org/10.3389/fonc.2023.1226652

[95] Takeuchi, K. (2012) Pathogenesis of NSAID-Induced Gastric Damage: Importance of Cyclooxygenase Inhibition and Gastric Hypermotility. *World Journal of Gastroenterology*, **18**, 2147-2160. https://doi.org/10.3748/wjg.v18.i18.2147