

睾丸间质干细胞的研究进展

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摘要 睾丸间质干细胞(stem leydig cells, SLCs)是位于睾丸组织生精小管外侧壁的一类成体干细胞, 具有维持自我更新和分化的特征。其分化形成的成熟间质细胞(adult leydig cells, ALCs)可以大量合成和分泌睾酮, 是雄性动物机体睾酮产生的主要来源, 广泛参与雄性动物的生殖和生理调控。由于SLCs发现较晚, 在特异性标记及潜在调控机制和临床应用等方面的研究还并不深入。该文主要对SLCs的起源、分子标记、自我增殖和分化机制以及临床应用等进行综述, 以促进SLCs研究和为雄性激素缺乏所引起疾病的临床应用奠定基础。

关键词 睾丸间质干细胞; 睾酮; 分子标记; 增殖和分化

Research Progress of Stem Leydig Cells

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Abstract SLCs (stem leydig cells) are a kind of adult stem cells, located in the lateral wall of seminiferous tubules in testicular tissue. They maintain the balance of self-renewal and differentiation. ALCs (adult leydig cells) differentiated from SLCs can synthesize and secrete large amounts of testosterone which are the main source of testosterone production in male animals. ALCs are widely involved in the regulation of reproduction and physiology in the male animals. Due to the late discovery of SLCs, studies on specific markers, potential regulatory mechanism and clinical application are not in-depth. In this paper, the origin, molecular markers, self-renewal, differentiation mechanism and clinical application of SLCs will be reviewed, so as to promote the study of SLCs and the clinical application of SLCs in the treatment of diseases caused by androgens deficiency.

Keywords stem leydig cells; testosterone; molecular markers; proliferation and differentiation

睾丸间质干细胞(stem leydig cells, SLCs)是一类位于生精小管外侧壁的干细胞, 呈纺锤状, 含有少量的滑面内质网, 可以维持自我更新和分化的动态平衡, 但不能合成和分泌睾酮^[1]。SLCs的起源和相关调控机制研究还不清楚, 以往很多研究一度把SLCs误认为是睾丸来源的多能干细胞, 主要是因为其具有类似多能干细胞的形态和标记^[2]。在一些物

种研究中, 也有很多学者误把它认为是雄性生殖干细胞(male germline stem cells, mGSCs)^[3], 这些错误的认识也说明, 关于SLCs的相关功能性研究还并不深入。

成熟间质细胞(adult leydig cells, ALCs)是SLCs分化的终末细胞, 可以大量合成和分泌睾酮, 是雄性动物机体内睾酮分泌维持稳定的主体细胞, 对雄性

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动物生殖系统的发育和功能维持起着重要的调控作用。在人的临床研究中发现,随着年龄的增长,成年男性体内的睾酮水平会逐渐下降,当血清中睾酮含量低于正常值时会引起雄性激素缺乏综合征(late onset hypogonadism, LOH)^[4],主要表现为性功能障碍、精子发育停滞和生殖能力下降等症状^[5]。目前治疗LOH的有效手段是睾酮激素补充疗法,但长时间补充睾酮,并不能根治。有研究显示,应用SLCs移植治疗LOH的方法具有较好的应用前景^[6],但目前关于SLCs移植治疗LOH的研究还并不多。本文将重点综述SLCs的来源、分子标记、自我增殖和分化机制以及临床应用等研究进展,以促进SLCs研究和临床应用,为雄性激素缺乏所引起疾病的治疗奠定基础。

1 睾丸发育与间质干细胞起源

具有大量睾酮合成和分泌功能的间质细胞(leydig cells, LCs)分为胚胎时期间质细胞(fetal leydig cells, FLCs)和成年期的ALCs。研究表明,FLCs和ALCs的来源和生成方式存在很大差异^[7]。FLCs起源有多种说法,可能来源于胚胎时期性腺原基表达类固醇生成因子-1(steroidogenic factor-1, SF-1)的间质细胞,也可能来源于性腺和中肾交界处的细胞^[8]。FLCs具有合成和分泌雄烯二酮的功能,在胚胎时期能促进雄性生殖系统的发育^[9]。一些研究显示,FLCs在雄性动物出生后会逐渐退化,且在成年小鼠中仍然存在,但是由于其合成和分泌的雄激素量过少,对成年小鼠机体的调控作用微乎其微^[7]。在灵长类新生儿时期,随着FLCs的退化一些新的睾丸间质类细胞形成并发育,但由于存在的时间很短,较难分离和鉴定,相关研究还有待深入解析^[7]。关于SLCs的起源,有学者认为其在胚胎发育时期就已经存在^[7]。从胚胎时期分离出的表达*Hes1*和*Gli1*基因的细胞在体外可分化为FLCs和ALCs亚群^[8]。但也有研究显示,雄性动物出生后7天才能分离得到SLCs,同时使用乙烯二甲基磺酸(ethane dimethane sulfonate, EDS)特异性去除ALCs,SLCs可以重新增殖并分化成为ALCs,显示SLCs是出生后才逐渐形成并一直存在着的,是ALCs来源的干细胞^[10]。这些研究表明,SLCs的起源还并不清楚,是否在胚胎期向FLCs分化等,还缺乏相关证据和研究,仍需要进一步探索。

在雄性动物青春期后,由于SLCs大量分化为

ALCs,使得雄性动物体内睾酮水平持续增多,最终维持在一定的水平^[11],这个过程对于精子成熟和雄性动物骨骼、肌肉功能的维持等都起到了重要的调控作用^[12]。

2 睾丸间质干细胞分子标记

SLCs表达多种多能干细胞和生殖干细胞的分子标记,同时也表现出具有多向分化的干细胞特征。研究发现,SLCs表达SF-1、类固醇激素合成急性调节蛋白(steroidogenic acute regulatory protein, StAR)、整合素 $\alpha 6$ (integrin $\alpha 6$, ITGA6)、阶段特异性胚胎抗原1(stage specific embryonic antigen 1, SSEA1)、白血病抑制因子受体(leukaemia inhibitory factor receptor, LIFR)和血小板衍生生长因子受体 α 亚基(platelet derived growth factor receptor alpha, PDGFR α)等标记物(表1),但不表达LCs谱系分子^[13]。在人类、猕猴、大鼠和小鼠的胎儿时期睾丸间质中的干细胞表达鸡卵清蛋白上游启动转录因子II(chicken ovalbumin upstream promoter transcription factor II, COUP-TFII)和核转录因子GATA4^[11]。在转基因小鼠中分离出巢蛋白启动GFP表达(*Nestin*-GFP⁺)的细胞是SLCs^[13];GE等^[10]用PDGFR α 膜抗原通过免疫技术成功分离获得出生后7天的大鼠SLCs;另外,通过使用CD51-PE免疫染色法分离获得出生后7天小鼠的SLCs,其纯度超过97%^[14]。这些结果显示了SLCs在睾丸中特异性表达NESTIN、PDGFR α 和CD51等蛋白。此外,研究报道,细胞外基质相关蛋白[COL6A3(collagen, type VI, $\alpha 3$)和FBN2(canine fibrinogen 2)]、钙黏蛋白2(cadherin 2, CDH2)和Notch信号通路相关蛋白(FURIN、FHL1和MCAM)等在SLCs中高水平表达。在灵长类的SLCs中也表达mGSCs和多能干细胞的分子标记,如GPR125、THY-1(CD90)、ITGA6、SSEA4和TRA-1-81等,这些标记物也是造成SLCs、mGSCs和多能干细胞混淆的主要原因^[2]。

间充质干细胞(mesenchymal stem cells, MSCs)是一种典型的成纤维细胞样的多能干细胞,分布在多种组织和器官中,具有分化为多种组织细胞的能力,且免疫原性低。研究发现,MSCs的特征性标志蛋白CD29、CD44、CD51、CD73、CD90、CD105和CD166,这些分子标志物也在SLCs膜表面表达^[3],而且SLCs也具有脂肪和成骨细胞的分化能力^[14],展现出类似于MSCs的分子特征。同时,很多研究显示,

表1 睾丸间质细胞的分子标记
Table 1 Molecular markers of leydig cells

细胞类型 Cell types	物种 Species	分子标记 Molecular markers	参考文献 References
SLCs	Mouse/rat	COUP-TFII, GATA4, LIFR, KIT, SF-1, CD51, CD90, PDGFR α , NESTIN	[10,14,18]
	Pig	SSEA1, SSEA4, CD29, PGP9.5, NANOG, TRA-1-60, TRA-1-81, GATA4, PDGFR α , LIFR, CYP11A1, CYP17A1, StAR, NESTIN, CD44, CD51, CD73, CD105, CD90	[3,19]
	Primates	GPR125, ITGA6, SSEA4, TRA-1-81, GFR- α , STRO-1, CD44, CD90, CD73, CD105, CD166, CD271, VCAM1, VIMENTIN, PGP9.5, OCT4, NANOG	[2,16,20]
PLCs	Rat	LHR, COUP-TFII, StAR, SF-1, 3 β -HSD, 3 α -HSD, CYP17A1, CYP11A1, HS-D3B1, KIT, PDGFR α , SRD5A1	[10,21]
	Pig	PGP9.5, SSEA1, SSEA4, NANOG, TRA-1-60, TRA-1-81	[3]
ILCs	Rat	HSD11 β 1, HSD17 β 3, CYP11A1, CYP17A1, 3 α -HSD, 3 β -HSD, SRD5A1, INSL3, NR5A1, StAR	[17,21-22]
ALCs	Mouse/rat	LHR, SF-1, 3 β -HSD, 3 α -HSD, 17 β -HSD, CYP11A1, CYP17A1, StAR, 11 β -HSD1, HSD3 β 6, HSD17B3, HSD11B1, CYP2A1, CYP2A2, CYP2A3, APOC1	[11,15,17,23]
	Human	GATA4	
FLCs	Mouse/rat	CYP11A1, CYP17A1, HSD3 β 1, INSL3, LHR, TSP 2, StAR, SF-1, GATA4	[6,11,23]

SLCs也被称为睾丸中的间充质干细胞(testis derived mesenchymal stem cells, tMSCs)^[2,16]。在SLCs与骨髓MSCs基因表达分析中, 显示出这两类细胞存在较小的差异, 其中Notch信号基因(*NOTCH1*和*MEF5*等)和*TNN*、*CD68*、*FCGR2A*以及*LAPTM5*等基因在骨髓MSCs中高水平表达; 而*DES*、*C2CD4D*和*RGDI566401*等基因在SLCs中也高水平表达^[15], 这些研究均显示, SLCs与骨髓MSCs在功能和基因表达方面极为接近。

SLCs不表达类固醇合成相关的酶类和促黄体生成素受体(luteinizing hormone receptor, LHR), 故不能合成和分泌睾酮^[10]。由SLCs最早分化生成的睾丸间质祖细胞(progenitor leydig cells, PLCs), 开始表达类固醇代谢的生物合成酶, 包括P450侧链裂解酶(P450_{scc}, 即CYP11A1)和低水平的LHR等(表1)^[15], 进一步分化为未成熟睾丸间质细胞(immature leydig cells, ILCs), 促使睾酮合成^[14]。从PLCs到ILCs分化过程中, 上调表达*PAH*、*CLIC6*、*C4B*、*CYP4F4*和*HSD17 β 3*等基因^[15]; 在睾酮合成过程中酶代谢活性不断增强, 主要包括3 α -类固醇脱氢酶(3 α -hydroxysteroid dehydrogenase, 3 α -HSD)和类固醇-5 α -还原酶等^[17]。从ILCs到ALCs分化过程中, 类固醇代谢酶的相关基因*CYP2A1*、*CYP2A2*、*CYP2A3*和*APOC1*等表达显著上调, 3 β -HSD和胰岛样因子3(insulin-like factor 3, INSL3)的表达水平也显著升高^[15]。

3 睾丸间质干细胞增殖与分化调控

SLCs具有维持自我更新和向类固醇代谢功能细胞分化的能力^[24], 是维持血液睾酮含量稳定的主要原因, SLCs逐步分化为PLCs、ILCs和ALCs, 最终ALCs进入老化和凋亡, 在此过程中涉及了许多基因和信号分子的调控(图1)^[25]。影响SLCs增殖和分化信号通路主要包括KIT(c-kit)、转化生长因子 β (transforming growth factor β , TGF β)、沙漠刺猬因子(desert hedgehog, DHH)、血小板衍生生长因子(platelet-derived growth factor, PDGF)、白血病抑制因子(leukaemia inhibitory factor, LIF)等信号通路, 这些信号通路激活和关闭, 影响SLCs增殖和分化状态。

3.1 KIT信号通路

在睾丸中, 由支持细胞分泌的干细胞因子(stem cell factor, SCF即KITL)与SLCs表达酪氨酸激酶受体c-kit结合形成KITL-KIT, 激活PI3激酶信号通路, 促使SLCs的StAR蛋白表达, 诱导SLCs分化和睾酮合成^[21]。较高浓度的KITL能促进SLCs的自我更新, 抑制类固醇代谢生成酶CYP11A1、CYP17A1和HSD17 β 3的表达和SLCs的分化^[21]。

3.2 TGF β 超家族信号通路

TGF β 1、AMH、激活素A和抑制素均为TGF β 超家族成员。TGF β 1可以刺激SLCs的增殖, 抑制SLCs分化^[25]。AMH在PLCs中通过与AMHII型受体结合激活受体样激酶, 降低LHCGR和CYP17A1的表

达水平,进而减少类固醇生成,抑制其PLCs增殖^[7]。激活素A与SLCs和PLCs膜上受体结合后促使SMAD蛋白磷酸化,刺激SLCs和PLCs增殖^[26];抑制素具有抑制SLCs增殖的作用^[11]。

3.3 DHH信号调控

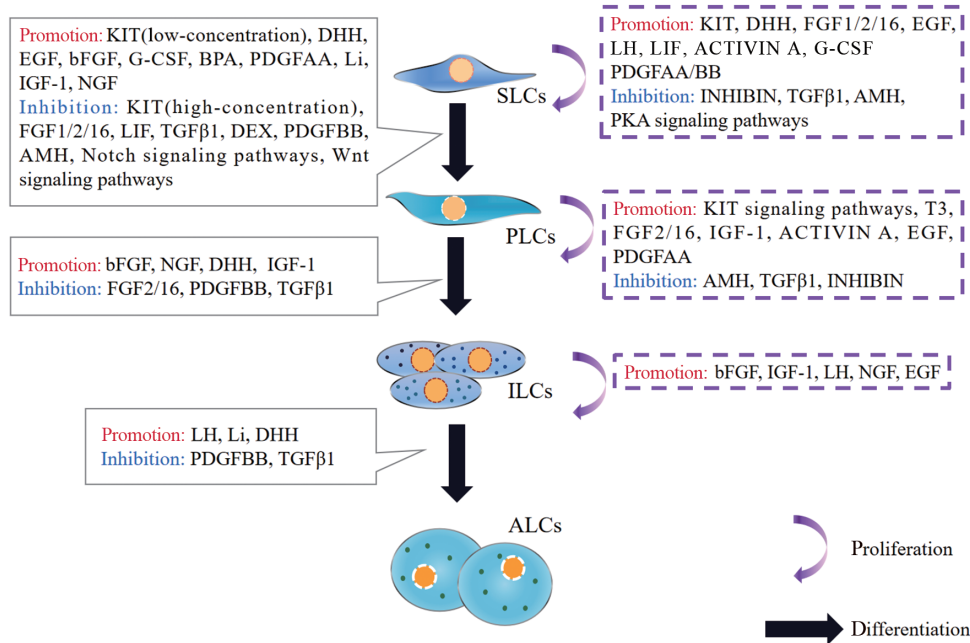
DHH被认为是开启SLCs分化的关键因子^[25],DHH信号可通过上调SF-1和CYP11A1的表达,诱导SLCs分化^[27]。DHH与PTCH1受体结合对FLCs的生成也具有重要的促进作用,DHH突变或缺失会导致雄性小鼠假两性畸形^[28]。此外,DHH相关的类固醇代谢调节因子WT1,在促进CYP11A1、CYP17A1、3 β -HSD和StAR等表达中起到加速SLCs分化的作用^[29]。实验表明,DHH或DHH激活剂SAG与其他调节因子(如PDGFBB或FGF2或激活素)联合使用时,睾酮生成量比只用锂或者LH处理要高得多,证明DHH对SLCs分化成ALCs、对类固醇合成都具有重要的促进作用^[25]。

3.4 PDGF信号通路

PDGFAA和PDGFBB是PDGF的两个二聚体,

分别与在SLCs上对应的受体PDGFR α 和PDGFR β 结合,均能促进SLCs增殖^[10];在SLCs分化过程中根据PDGF二聚体种类不同而具有双向作用,PDGFAA与PDGFR α 结合可促进SLCs分化,PDGFBB与PDGFR β 结合则抑制SLCs分化^[25]。在LCs中类固醇生成细胞里PDGF通路的两个成员(*SGP11*和*PLEKHA1*)可以激活类固醇代谢调控^[12],*PDGFR α* 基因敲除的小鼠ALCs分化停滞^[30]。因此,PDGF信号是SLCs向ALCs分化的一个重要调控通路。PDGFR α 信号通路也可以促进FLCs的生成^[24]。

LIF是白细胞介素细胞因子家族的成员之一,通过介导JAK-STAT3和促分裂原活化蛋白激酶(mitogen-activated protein kinase, MAPK)信号通路促进SLCs的增殖^[17]。成纤维细胞生长因子-1(fibroblast growth factor-1, FGF-1)^[31]、FGF-2^[32]、FGF-16^[33]和DEX(dexamethasone)^[34]可促进SLCs和PLCs增殖,降低LHCGR、SCARB1、CYP11A1、HSD17 β 3、HSD11 β 1和HSD3 β 1等类固醇合成酶的表达,进而抑制SLCs分化。其中*FGF-9*敲除的LCs发育不全,发生



KIT: 干细胞因子受体; DHH: 沙漠刺猬因子; EGF: 表皮生长因子; FGF1/2/16: 成纤维细胞生长因子家族成员; G-CSF: 粒细胞集落刺激因子; BPA: 双酚A; PDGFAA/PDGFBB: 血小板衍生生长因子的二聚体AA/BB; LIF: 白血病抑制因子; TGF β 1: 转化生长因子 β 1; DEX: 地塞米松; LH: 促黄体生成素; T3: 甲状腺激素; IGF-1: 胰岛素样生长因子1; NGF: 神经生长因子; AMH: 抗苗勒激素。

KIT: the receptor of stem cell factor; DHH: desert hedgehog; EGF: epidermal growth factor; FGF1/2/16: the family of fibroblast growth factor; G-CSF: granulocyte-colony stimulating factor; BPA: bisphenol A; PDGFAA/PDGFBB: platelet-derived growth factor AA/BB; LIF: leukaemia inhibitory factor; TGF β 1: transforming growth factor β 1; DEX: dexamethasone; LH: luteinizing hormone; T3: thyroid hormone; IGF-1: insulin-like growth factor-1; NGF: nerve growth factor; AMH: anti-müllerian hormone.

图1 影响睾丸间质干细胞增殖分化的因素

Fig.1 Factors influencing the proliferation and differentiation of SLCs

性别反转^[33]。FGF-16通过激活PI3K激酶使AKT1/2、ERK1/2蛋白磷酸化而发挥调控作用^[33]。表皮生长因子(epidermal growth factor, EGF)^[35]和双酚A^[36]可以通过上调StAR、3 β -HSD、CYP11A1和HSD17 β 3等类固醇合成酶的表达,促进睾酮合成和诱导SLCs分化。神经生长因子(nerve growth factor, NGF)通过酪氨酸激酶受体A和p75神经营养素受体介导刺激SLCs-PLCs-ILCs分化调控^[37],通过增强StAR和CYP11A1的表达,从而促进睾酮合成^[38]。

4 睾酮合成与分泌调控

睾酮是胆固醇在ALCs中由睾酮合成相关酶催化和加工所产生的。对雄性生殖器官的发育、功能维持、机体的新陈代谢、肌肉质量以及骨质密度具有重要作用^[14]。受下丘脑-垂体-性腺轴(hypothalamic-pituitary-gonadal axis, HPGA)的调控^[39]。睾酮缺乏会直接影响人的情绪和认知能力^[40],增加患糖尿病和粥样硬化等疾病的概率。随年龄的增加,类固醇代谢功能逐渐降低,促使血液中睾酮含量减少^[23]。

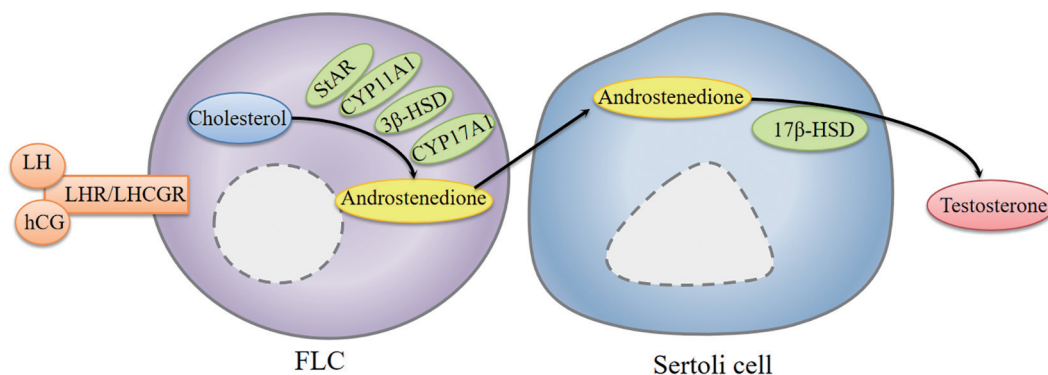
在胚胎时期,睾酮的合成与分泌需要由FLCs和支持细胞的参与才能完成(图2)^[9]。FLCs中的胆固醇在StAR、CYP11A1、3 β -HSD、CYP17A1的作用下形成雄烯二酮,进入支持细胞中,受催化的17 β -HSD转化成睾酮。不同物种合成与分泌睾酮所受到的激素调控也不同,啮齿动物(大鼠、小鼠)睾酮的合成独立于HPGA^[41],不需要促黄体生成素(luteinizing hormone, LH)调控^[42]。灵长类动物(包括人类)睾酮早期合成独

立于HPGA会依赖人绒毛膜促性腺激素(human chorionic gonadotropin, hCG)调控,后期依赖LH^[41,43]。

青春期以后,睾酮的合成与分泌主要由ALCs完成(图3)^[44]。合成途径与胚胎时期类似,不同的是,ALCs中表达17 β -HSD,不需要支持细胞参与;而ALCs睾酮的合成与分泌主要依赖HPGA并通过LH或hCG调控^[45],也可以依赖胰-骨-睾丸轴,通过骨钙素(osteocalcin, Os)调控^[46]。

5 睾丸间质干细胞临床应用

随着人口老龄化发展趋势和生活压力的增大,LOH和中老年男性雄激素部分缺乏综合征(partial androgen deficiency of the aging male, PADAM)不断地发生^[47]。其中,LOH相关性疾病主要是由SLCs损伤和睾酮分泌不足引起的,促使ALCs数量减少或功能下降^[48-49]。研究显示,将SLCs移植到老年灵长类动物体内,睾酮水平明显升高,有助于改善雄激素缺乏^[20]。研究显示,SLCs移植为治疗睾酮缺乏症提供了新的见解,在这项研究中通过体外培养从小鼠睾丸中分离的SLCs,发现CD51可以作为该细胞的标志物,并且它们可以生理性恢复睾丸的内分泌功能^[50]。也有研究显示,SLCs在体外具有自我更新和多向分化的能力,能在一定作用下分化为多种类型细胞^[13]。SLCs移植可部分恢复鼠LCs分化和衰老动物中睾丸激素水平,促进睾酮分泌的恢复和产生^[13]。SLCs自体移植可以提高血清睾酮含量^[51]。这些研究均显示了SLCs治疗睾酮缺乏和雄激素分泌不足具有良好

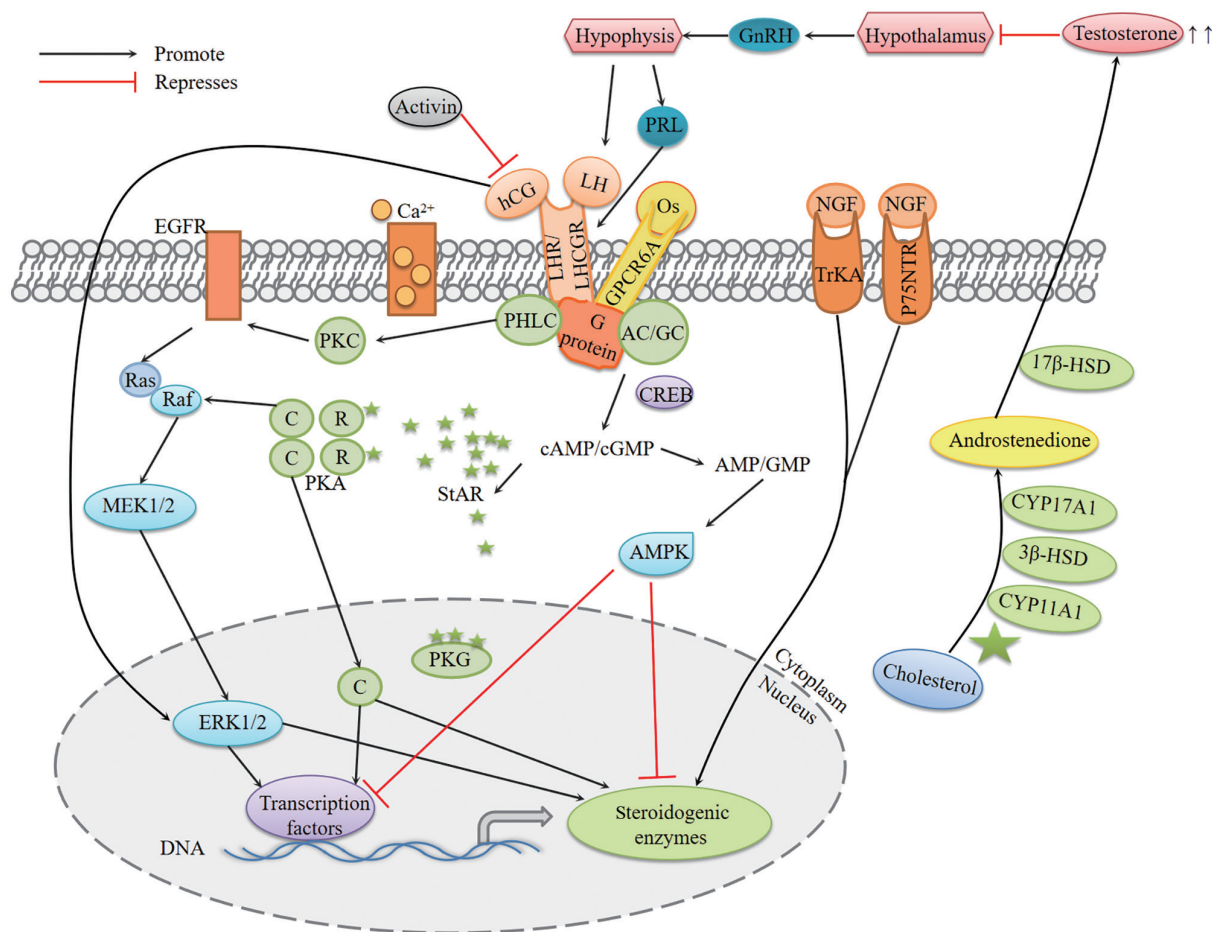


StAR: 类固醇激素合成急性调节蛋白; CYP11A1: P450侧链裂解酶; CYP17A1: 细胞色素P450 17 β -羟化酶; 3 β -HSD: 3 β -羟类固醇脱氢酶; 17 β -HSD: 17 β -羟类固醇脱氢酶; LH: 促黄体生成素; hCG: 人绒毛膜促性腺激素; LHR/LHCGR: 促黄体生成素受体/绒毛膜促性腺激素受体。

StAR: steroidogenic acute regulatory protein; CYP11A1: P450 side-chain cleavage enzyme; CYP17A1: cytochrome P450 17 β -hydroxylase; 3 β -HSD: 3 β -hydroxysteroid dehydrogenase; 17 β -HSD: 17 β -hydroxysteroid dehydrogenase; LH: luteinizing hormone; hCG: human chorionic gonadotropin; LHR/LHCGR: luteinizing hormone receptor/human chorionic gonadotropin receptor.

图2 胚胎期FLCs睾酮合成与分泌调控

Fig.2 Regulation of testosterone synthesis and secretion of FLCs in embryo



GnRH: 促性腺激素释放激素; PRL: 催乳素; LH: 促黄体生成素; AMH: 抗苗勒激素; hCG: 人绒毛膜促性腺激素; Os: 骨钙素; PHLC: 磷脂酶C; AC: 腺苷酸环化酶; GC: 鸟苷酸环化酶; LHR/LHCGR: 促黄体生成素受体/绒毛膜促性腺激素受体; EGFR: 表皮生长因子受体; TRKA: 酪氨酸激酶受体; p75NTR: p75神经生长因子受体; PKA: 蛋白激酶A(C: 催化亚基, R: 调节亚基); PKC: 蛋白激酶C; NGF: 神经生长因子; cAMP: 环磷酸腺苷; cGMP: 环磷酸鸟苷; AMP: 一磷酸腺苷; GMP: 一磷酸鸟苷; AMPK: AMP激活蛋白激酶; PKG: 蛋白激酶G; MEK1/2: 促分裂原活化蛋白激酶激酶1/2; ERK1/2: 促分裂原活化蛋白激酶1/2; CREB: 环磷酸腺苷效应元件结合蛋白; GATA4: GATA结合蛋白4; StAR: 类固醇激素合成急性调节蛋白; CYP11A1: P450侧链裂解酶; CYP17A1: 17 α -羟化酶; 3 β -HSD: 3 β -羟类固醇脱氢酶; 17 β -HSD: 17 β -羟类固醇脱氢酶。↑↑: 升高。

GnRH: gonadotrophin releasing hormone; PRL: prolactin; LH: luteinizing hormone; AMH: anti-Mülleria hormone; hCG: human chorionic gonadotropin; Os: osteocalcin; PHLC: phospholipase C; AC: adenylate cyclase; GC: guanylate cyclase; LHR/LHCGR: Luteinizing hormone receptor/human chorionic gonadotropin receptor; EGFR: epidermal growth factor receptor; TRKA: tyrosine kinaseA; p75NTR: p75 neurotrophin receptor; PKA: protein kinase A (C: regulatory subunit, R: regulatory subunit); PKC: protein kinase C; NGF: nerve growth factor; cAMP: cyclic adenosine monophosphate; cGMP: cyclic guanosine monophosphate; AMP: Adenosine monophosphate; GMP: guanosine monophosphate; AMPK: AMP-activated kinase; PKG: protein kinase G; MEK1/2: extracellular-regulated kinase kinase 1/2; ERK1/2: extracellular-regulated kinase 1/2; CREB: cAMP-response element binding protein; GATA4: GATA binding protein 4; StAR: steroidogenic acute regulatory protein; CYP11A1: P450 side-chain cleavage enzyme; CYP17A1: 17 α -hydroxylase; 3 β -HSD: 3 β -hydroxysteroid dehydrogenase; 17 β -HSD: 17 β -hydroxysteroid dehydrogenase. ↑↑: increasing.

图3 成年期ALCs睾酮合成和分泌调控

Fig.3 Regulation of testosterone synthesis and secretion of ALCs in adulthood

临床效果,但目前相关研究报道还太少,仍需要进一步探究。

6 展望

SLCs在睾丸生精小管侧壁上,可维持自我更新和分化,在多种因素的调控作用下可分化为ALCs,参与合成和分泌大量睾酮,这是雄性动物体内维持

睾酮水平恒定的关键因素,是调控男性生殖生理健康的基础。睾酮合成受阻或分泌不足会直接影响机体的正常生理功能,引发临床表现多种疾病。与药物补充疗法相比,SLCs移植治疗的方法更具有特异性和针对性,是临床应用中最具有希望的治疗方法。但SLCs的分子标记和调控机制研究还并不深入,极大程度限制了其在临床治疗中的应用,深入开展

SLCs的研究, 将有助于促进男性健康和生殖生理调控方面理论和临床的发展。

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