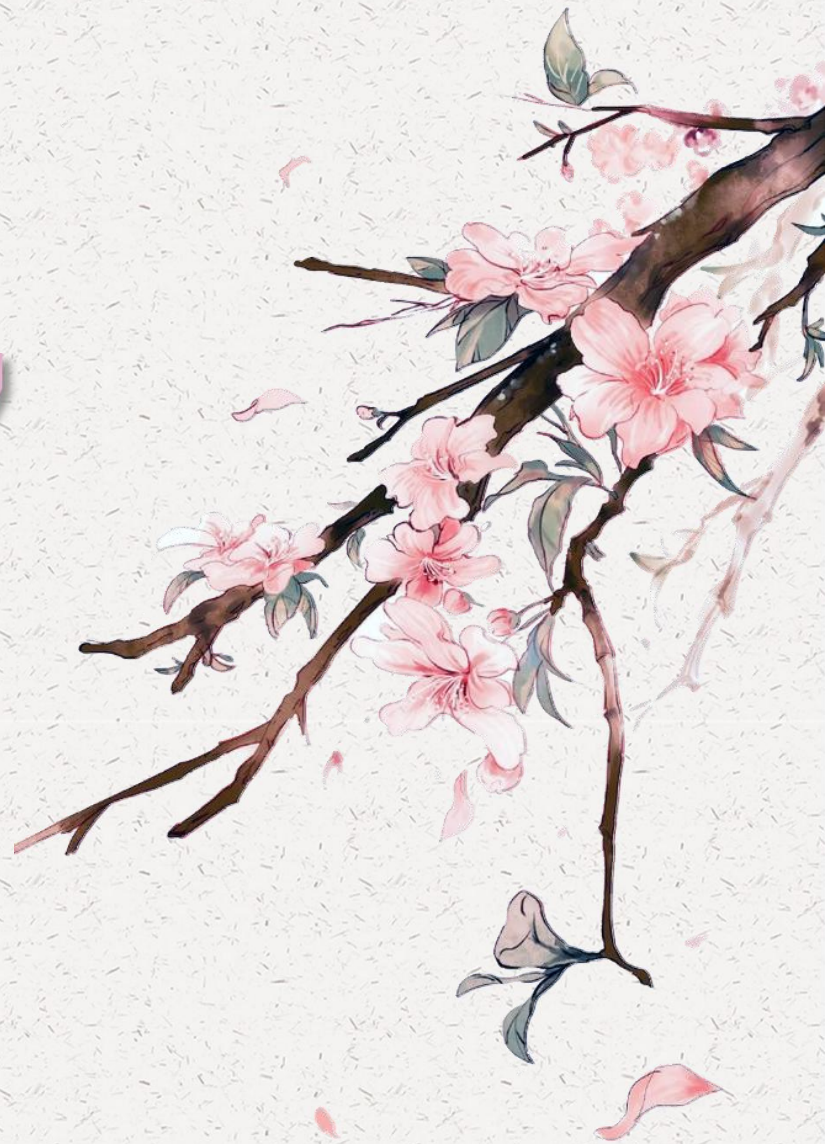
河南师范大学水产学院
College of Fisheries Henan Normal University

2017

读书报告



于若梦

World Journal of Gastroenterology

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Long-chain acyl-CoA synthetase in fatty acid metabolism involved in liver and other diseases: An update

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文章简介

长链酰基辅酶A合成酶（ACSL）家族成员包括五种不同的ACSL同种型，每种编码单独的基因并具有多个剪接变体。ACSLs内质网和线粒体外膜催化脂肪酸链长度为12至20个碳原子以形成酰基-Co As，它们是脂质代谢中间体并涉及在脂肪酸代谢，膜修饰和各种生理过程。增益或损失 - 功能研究已经表明了这个表达的个体ACSL同种型可以改变分布和细胞内脂肪酸的量。的变化脂肪酸的类型和数量又可以改变细胞内ACSLs的表达。 ACSL家庭成员不仅影响正常细胞的增殖，而且恶性肿瘤细胞增殖。他们也规范细胞凋亡通过不同的信号通路和分子机制。ACSL会员有个人功能不同类型的脂肪酸代谢细胞取决于底物偏好，亚细胞位置和组织特异性，从而有助于肝脏疾病和代谢疾病，如脂肪肝疾病，肥胖，动脉粥样硬化和糖尿病。他们也与神经系统疾病等有关疾病。然而机制尚不清楚。这个审查讨论了分类中的新发现ACSLs的性质和脂肪酸代谢 -ACSLs在疾病中的相关作用。

ACSL家族介绍

- ACSL1--分布与作用
- ACSL3--
- ACSL4--
- ACSL5--
- ACSL6--

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不同类型的ACSL在组织中的分布情况及其作用

名称	分布	作用
ACSL1	脂肪组织，肝和心脏	提供用于TAG合成的酰基辅酶A，线粒体β氧化
ACSL3	脑，骨骼肌和睾丸	介导脂肪生成转录控制的作用
ACSL4	肝，脑和肾上腺	
ACSL5	肝脏，十二指肠粘膜和棕色脂肪组织	
ACSL6	脑和骨骼肌	?

ACSL与疾病

- ACSL对细胞增殖的影响
- ACSL对细胞凋亡的影响
- ACSL与肝病
- ACSL与代谢疾病
- ACSL与神经系统疾病
- ACSL与其他疾病

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ACSL对细胞增殖的影响

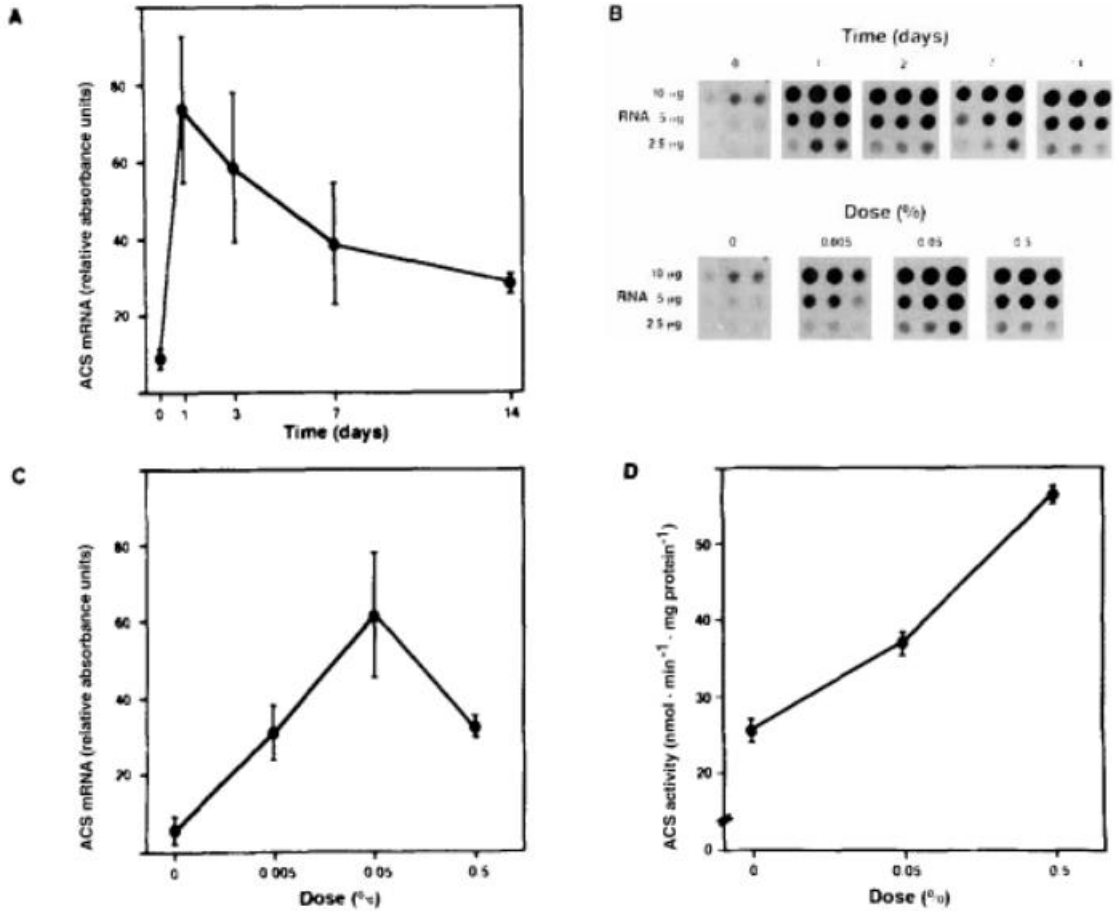


Fig. 2. Influence of fibrate treatment on adipose tissue ACS gene expression. (A) Effect of duration of treatment with fenofibrate on adipose tissue ACS mRNA levels. Adult rats were treated for the times indicated with 0.5% (by mass) fenofibrate. (B) Dot blots for samples obtained from animals used in the experiments depicted in (A) and (C). (C) Effect of treatment with different doses of fenofibrate on adipose tissue ACS mRNA levels. Adult male rats were treated for 14 days with the indicated doses (by mass) of fenofibrate in rat chow. (D) Effect of treatment with different doses of fenofibrate on adipose tissue ACS enzyme activity. ACS mRNA and activity levels were measured as described in Materials and Methods. Each bar represents the mean ± SD of three independent determinations.

ACSL对细胞凋亡的影响

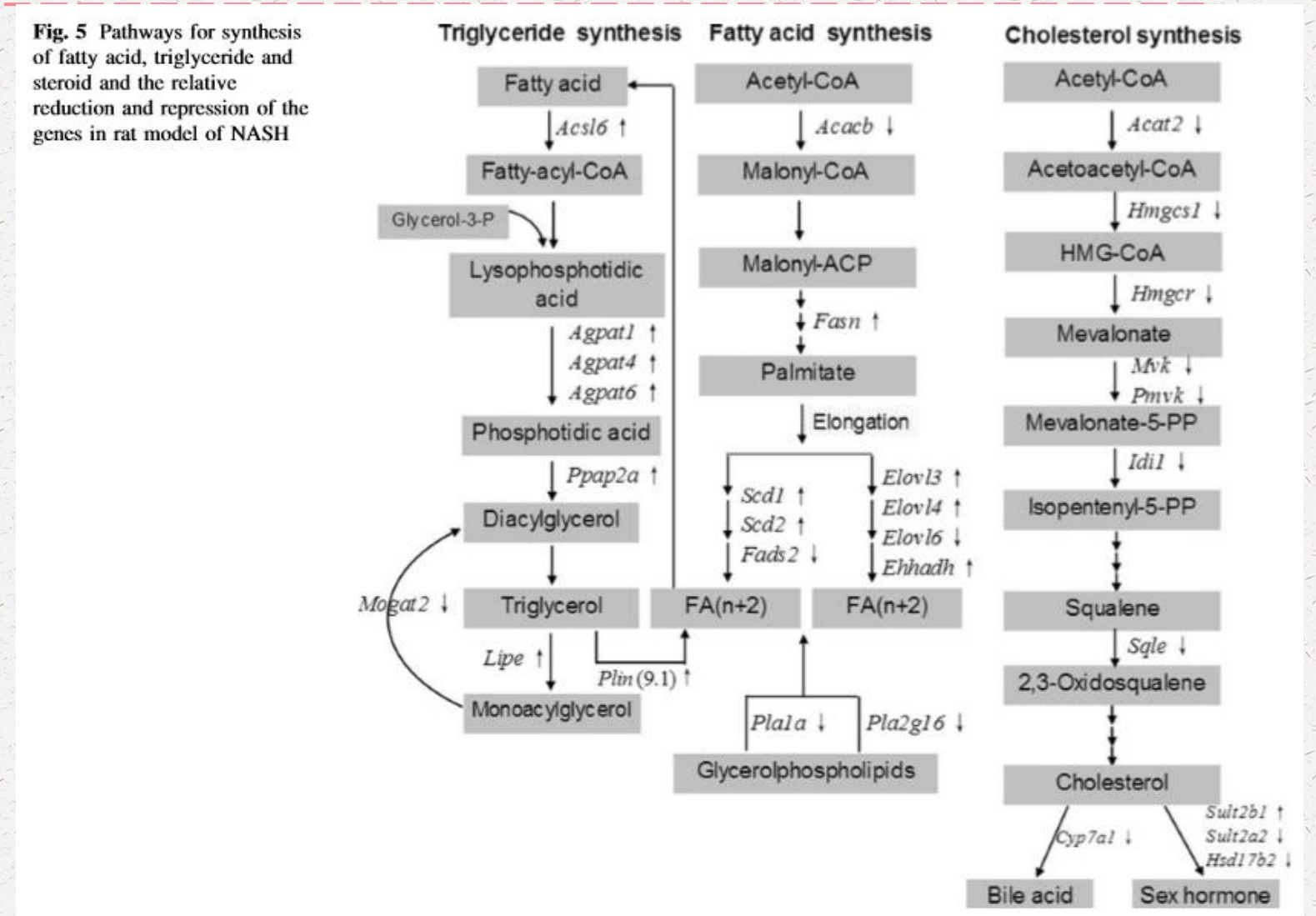


Fig. 5 Pathways for synthesis of fatty acid, triglyceride and steroid and the relative reduction and repression of the genes in rat model of NASH

ACSL与肝病

Table 1 Long-chain acyl-CoA synthetase expression and pathways involved in liver diseases

	Liver diseases	mRNA expression	Pathways	Ref.
ACSL1	HF	↓	PPAR/NF-κB/p65	Xin *et al*[39] and Pyper *et al*[42]
	NAFLD	↓	TGF	Uto *et al*[43]
ACSL3	NAFLD	↓	LXR/RXR	Dong *et al*[44]
ACSL4	HCV	↓	–	Yao *et al*[17]
	HCC	↑	P38/cAMP	Liang *et al*[32]
	NAFLD	↑	–	Stepanova *et al*[41]
ACSL5	NAFLD	↑	Caspase	Reinartz *et al*[40]

ACSL: Long-chain acyl-CoA synthetase; HF: Hepatic fibrosis; NAFLD: Non-alcoholic fatty liver disease; HCV: Hepatitis C virus; HCC: Hepatocellular carcinoma; PPAR: Peroxisome proliferator-activated receptor; NF-κB: Nuclear factor of kappa light polypeptide gene enhancer in B-cells; TGF: Transforming growth factor; LXR: Liver X receptor; RXR: Retinoid X receptor; cAMP: 3′-5′-cyclic adenosine monophosphate.

ACSL与代谢疾病

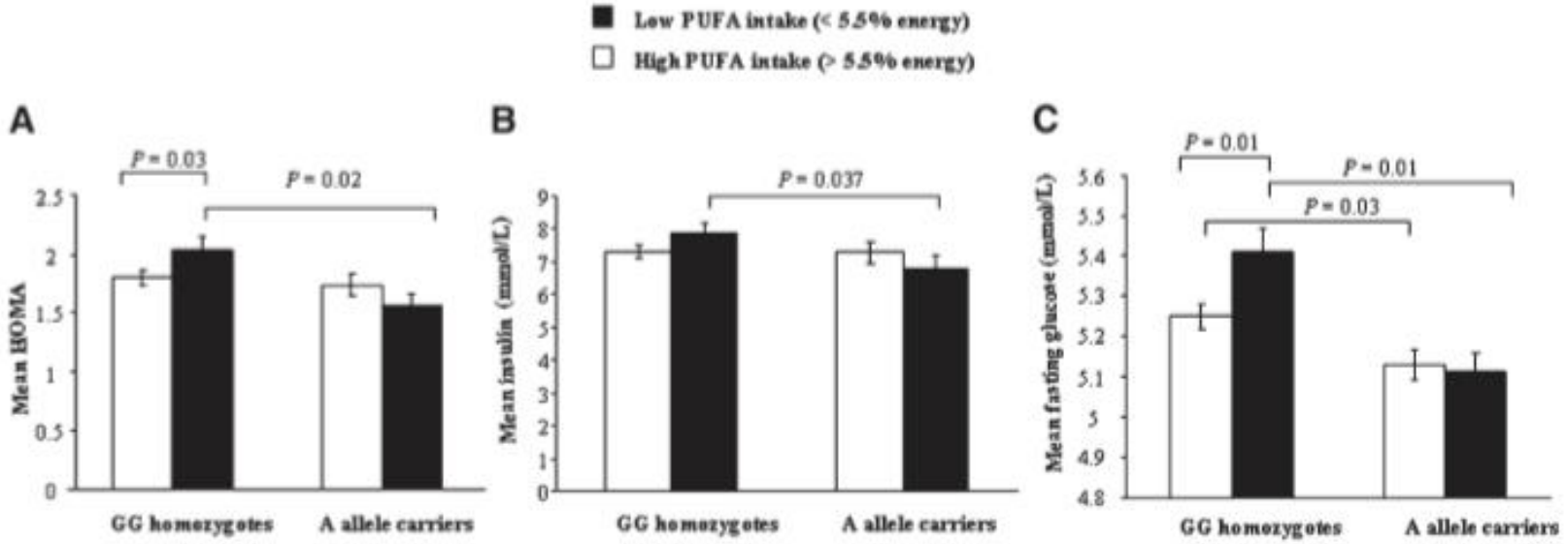
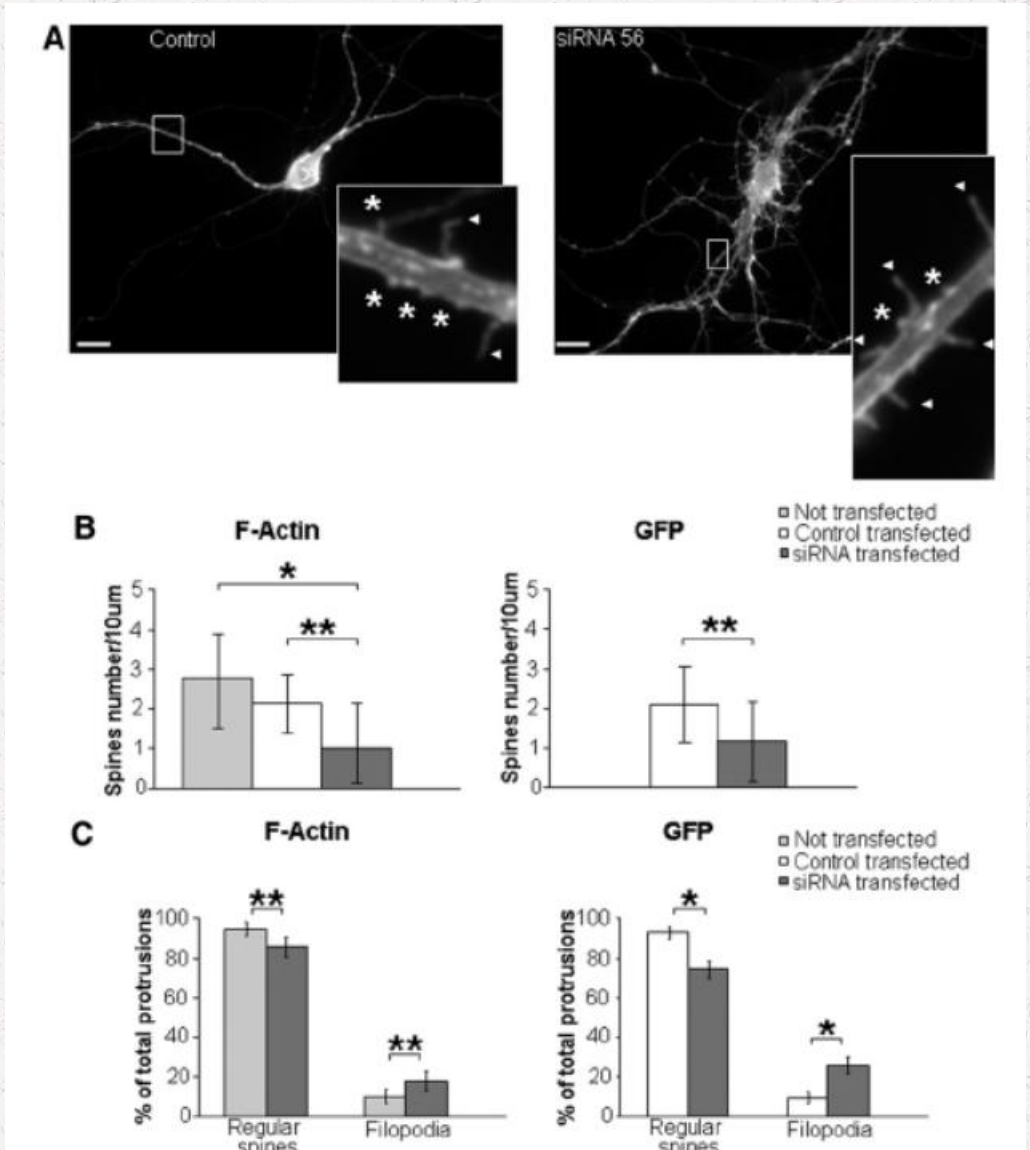


Fig. 1. Influence of *ACSL1* rs9997745 genotype and dietary PUFA status on insulin resistance as assessed by HOMA (A), fasting insulin (B), and glucose (C) concentrations. Values are means ± SEM. *P*-values for linear regression adjusted for potential confounding factors. When dietary PUFA intake was low (<5.5% energy), GG homozygotes (n = 848) displayed greater insulin resistance (A) and higher fasting insulin (B) and glucose (C) concentrations compared with the A allele carriers (n = 327). Furthermore, fasting glucose levels were significantly higher in the GG homozygotes with a low-PUFA intake compared with both GG homozygotes (n = 418) and A allele carriers (n = 161) with a high-PUFA intake. The detrimental effects conferred by GG homozygosity on insulin resistance and insulin concentrations were abolished against a high-PUFA background (>5.5% energy).

ACSL与神经系统疾病



ACSL与其他疾病

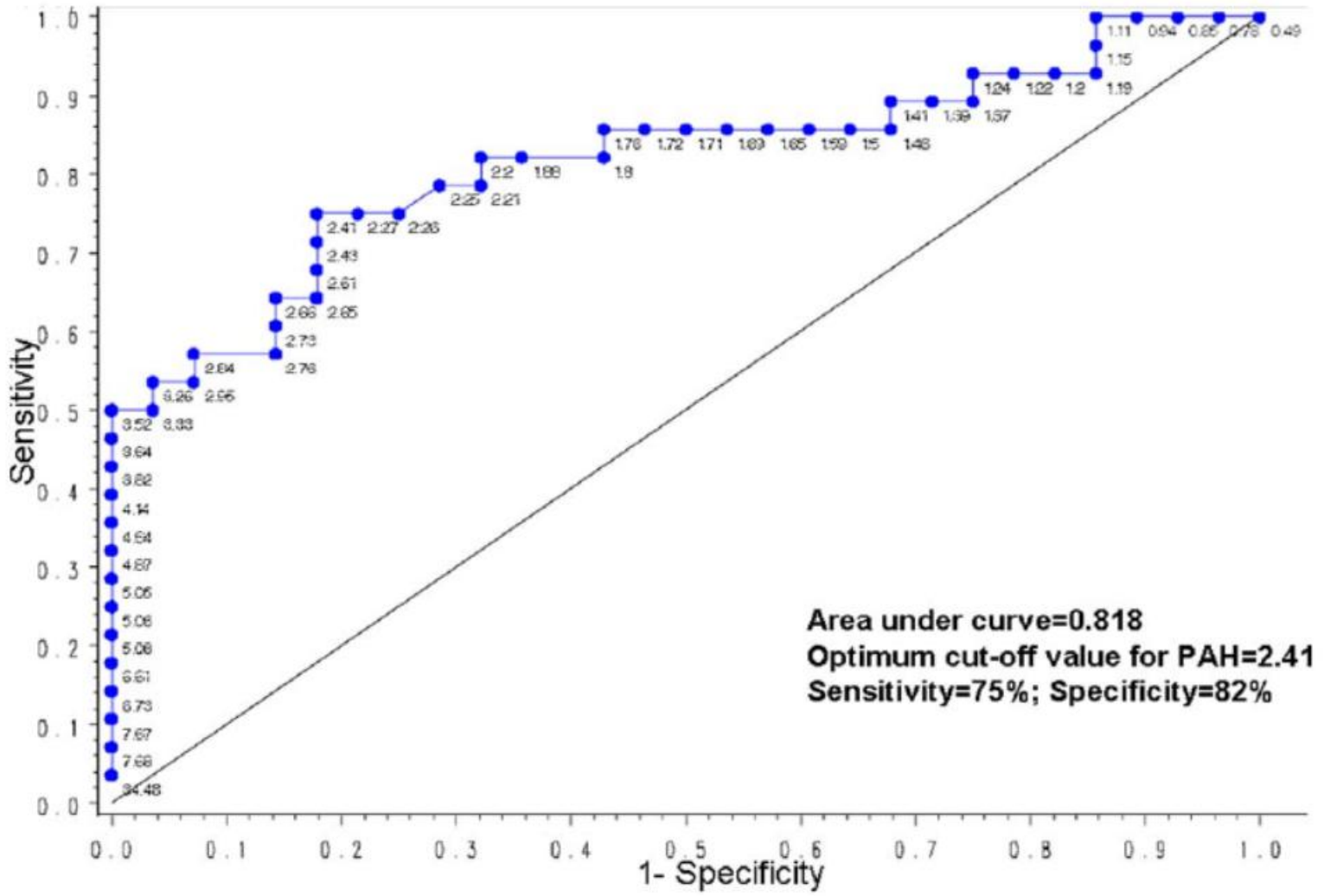


Figure 5. Receiver operating characteristics (ROC) plot for 56 children on PAH values and methylation status of *ACSL3* analyzed by MSPCR. Point labels are values of PAH of each children. Statistical software, sas, was used for ROC plot and R was used for determination of cutoff value. The cutoff value corresponds to the desired sensitivity and specificity (or 1-specificity).
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结论

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结论

ACSL在脂肪酸代谢中起关键作用。 脂肪酸，饱和或不饱和的，是人类的主要能源并且是必需的，特别是不饱和脂肪酸。需要活化脂肪酸以形成酰基Co在他们进入代谢途径之前，包括两者合成代谢途径和分解代谢途径。

最近的研究ACSL主要集中在对脂肪的影响酸代谢和对细胞的影响较小增殖和凋亡。涉及的机制在脂肪酸代谢和细胞增殖中凋亡不清楚。 进一步研究阐明ACSL酶的功能将是非常有益的。

敬请各位老师同学批评指正