上海市药理学会通讯

INFORMATION OF THE SHANGHAI PHARMACOLOGICAL SOCIETY

2016 年 10 月 25 日 **第 56 期**

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第二军医大学药理学教研室承办

主编：缪朝玉

编者：王　培　程明和　孙　旸

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祝贺陈宜张院士九十华诞

缪朝玉 第二军医大学药理学教研室

我 1981 年考上第二军医大学军医系时，就知道学校有位鼎鼎大名的教授叫陈宜张。因为陈教授是浙江余姚人，我是浙江奉化人，余姚与奉化相邻，我们称得上是宁波同乡，为此我感到很高兴。看到他，接触他，马上会联想到江南的书香门第，他的严谨、好奇、渊博……都给人深刻印象。甚至，在 2015 年屠呦呦获得诺贝尔奖，当我从媒体得知屠呦呦她那充满诗情画意色彩的姓名由来时，我的第一反应会联系到陈宜张院士。可见，陈院士在我心目中的形象和分量，他是我们浙江籍教育家和科学家的杰出代表。

陈宜张

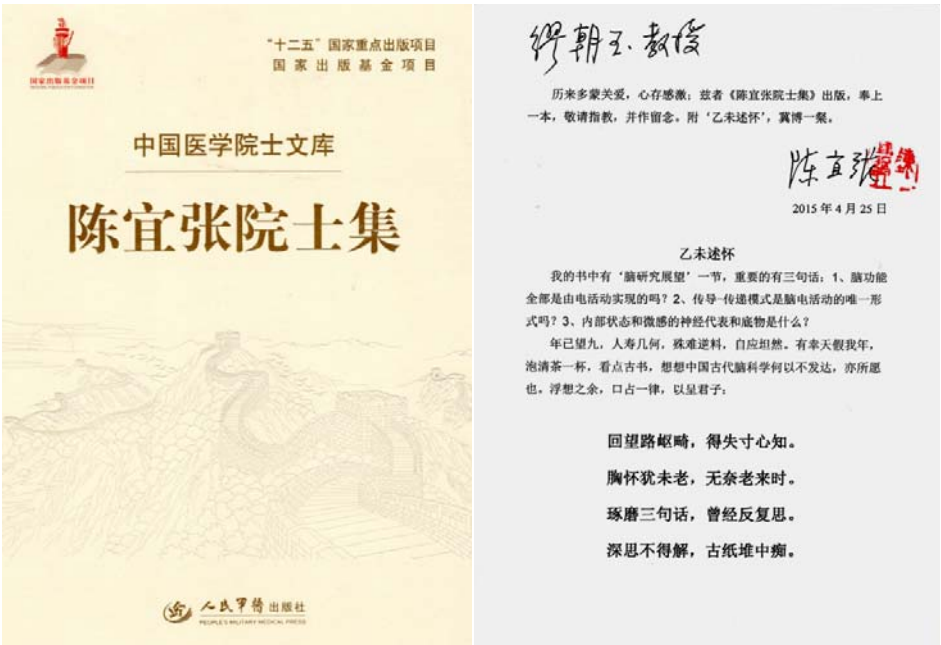
陈院士和他的夫人徐仁宝教授是我的老师，分别教我生理学和病理生理学。我读药理学研究生时，更加了解到他们夫妇在学术上的威望，比翼齐飞，可谓楷模。作为一代名师，陈院士醉心于教书育人，以教书匠为荣，工作六十五年来一直活跃在三尺讲台上。每次上课前，他都要精心备课，把最新的专业文献资料充实到讲课内容中，并用中英文讲解，充满激情，有声有色，把枯燥的基础医学课讲好讲活，感染在场的学生们，培养他们学习兴趣，启发他们独立思考。记得有一年冬天，天气很冷，陈院士应邀来到学生食堂，与我们军医系 81 级学员座谈。同学们挤挤一堂，围在陈院士身边，听他讲学习方法、谈科学态度，师生互动活跃，气氛热烈，陈院士的诲人不倦、宽广深厚的学术修养让我至今难忘。

陈宜张与军医系 81 级学员在食堂交流探讨问题(1985 年 1 月)

陈院士在神经生理学和神经内分泌学研究领域贡献卓越。我研究生毕业后留校工作，在讲授药理学“糖皮质激素”一课时，每次都很骄傲地提及，在该领域发展中，我校陈宜张院士提出了“糖皮质激素膜受体”概念，发挥了全球引领作用，因为先前认为这类甾体激素的受体只存在于细胞内，通过基因组发挥作用，而陈院士团队观察到糖皮质激素快速、非基因组作用，由此推想甾体激素存在新的细胞膜受体作用途径，直到后来他人寻找到甾体激素膜受体，彻底更新了这一领域的理论知识，并对临床实践产生了重要影响。读他近年发表的文章“活细胞大分子的定位和定量问题”，出版的专著《突触》，发行的文集《陈宜张院士集》，更让我体会到，他一直在学习，一直在深思，一直在贡献，“始终如一，永远在路上”。这些在他望九高龄用心血铸就的新作品，必将推进精确细胞生物学和脑科学研究的新发展。

陈宜张作为执行主席在科学与技术前沿论坛上致开幕词(2012 年 11 月)

生理学科与我们药理学科有着天然联系，以前我在基础医学部工作，生理与药理还是三楼与四楼近邻关系，陈院士等生理老前辈与我们药理老前辈谭世杰教授、顾科民教授交往密切。2003 年学科调整，基础医学部药理与药学院药理合并，成立新的药学院药理学教研室，每当我们药理取得一点进步，例如，我获得杰青、我当选主任、我们获得国家自然科学二等奖，都得到陈院士的极大鼓励，我铭记在心。当前我们两个学科虽属不同院系，但依然交往甚多，生理学科何成主任(神经生物学教研室)、倪鑫主任(生理学教研室)也都是我的好朋友、好同道。



在赠书扉页上，陈宜张提出三个脑科学问题，写诗一首

时间过得真快，陈院士给我们教课时的风采，陈院士夫妇在校园散步探讨学术的身影，陈院士 80 岁生日庆祝会的学术场面，陈院士在教授餐厅与我们中青年教师日常交流的亲切场景……历历在目，仿佛昨日。

喜逢 2016 年陈院士 90 华诞，在此衷心祝愿陈宜张院士和徐仁宝教授身体健康，福如东海，寿比南山！

缪朝玉

2016 年 10 月 23 日

中国药理学会第十四次全国学术大会暨中国药理学会-施维雅优秀青年药理学工作者奖20周年学术论坛召开

“中国药理学会第十四次全国学术大会暨中国药理学会-施维雅优秀青年药理学工作者奖20周年学术论坛”于2016年10月22-25日在北京国际会议中心召开。700余名代表参加了本次大会。

大会开幕式由中国药理学会副理事长兼秘书长张永祥教授主持，中国药理学会理事长杜冠华教授首先代表大会组委会致欢迎辞。国际药理学联合会（IUPHAR）主席S J Enna教授、IUPHAR副主席Masamitsu Iino教授、IUPHAR提名委员会主席Kim Brøsen教授、美国药理学与实验治疗学学会前主席Kenneth Thummel教授、亚洲太平洋药理学家联盟主席Masayoshi Mishina教授、香港中文大学容永豪教授、国家卫计委科教司重大专项处顾金辉处长等嘉宾参加开幕式并发表讲话。

10月24日下午，中国药理学会-施维雅优秀青年药理学工作者奖20周年庆典活动在学术大会期间召开。施维雅集团总裁Olivier Laureau先生、研发高级执行副总裁Emmanuel Canet博士、卓越药物与生物药学中心副总监Pierre Renard博士代表施维雅集团参加了庆典仪式并发表了讲话。林志彬教授和杜冠华教授代表中国药理学会，回顾了奖项设立和发展的历史，并对施维雅集团长期以来对中国药理学发展提供的帮助表示诚挚感谢。缪朝玉教授代表历届获奖者在庆典仪式上发言。来自双方共10位对本奖设立和发展做出了杰出贡献的专家获颁特殊贡献奖，并在庆典仪式上现场拓印手模，将气氛推向了高潮。

“中国药理学会-施维雅奖20周年学术论坛”在庆典仪式后举行，五位历届获奖者，包括上海健康医学院孙安阳教授、第二军医大学缪朝玉教授、中山大学肿瘤防治中心符立梧教授、安徽医科大学沈玉先教授和中国医学科学院药物研究所花芳博士，做了精彩的学术报告。他们的报告代表了历届获奖者的高水平学术造诣，获得了与会专家和代表的一致高度赞扬。

本次学术大会的胜利召开，标志着我国药理学事业的发展和国际认同性达到了一个新的高度。在新的时代，中国药理学会将秉承一贯以来的以学术为中心，

努力推动学科发展和国际交流，为人类健康和社会福祉作出更大贡献！（来源：中国药理学会网站）

缪朝玉教授在中国药理学会-施维雅青年药理学工作者奖20周年庆典仪式上发言

尊敬的施维雅集团总裁先生、各位贵宾和王萱博士：
尊敬的中国药理学会各位前辈、各位领导、各位同仁和各位朋友：
大家下午好！

我非常荣幸作为历届获奖者代表，在中国药理学会-施维雅青年药理学工作者奖20周年庆典上发言。首先向今年获奖者表示热烈祝贺！

中国药理学会-施维雅青年药理学工作者奖(以下简称施维雅奖)是由法国施维雅研究院与中国药理学会共同创立，颁发给在中国国内做出药理学研究成果的优秀年轻学者。除了获奖荣誉，每个获奖者还得到一笔丰厚的奖金。这个奖项对中国青年学者的成长起到了激励和引领作用。

20 年前当中国科研和生活条件还很差的时候，外国制药企业进入中国的很少，施维雅已经开始在中国帮助中国优秀的年轻科学家在中国贡献于中国的科研事业。现在中国发展了，市场大了，全世界的公司都到中国来了。但是，我们永远不会忘记在中国困难的时候，最需要帮助的时候，谁帮助了我们，那就是法国施维雅！谢谢法国施维雅！

我本人于 1999 年获得施维雅奖。作为获奖者之一，我对施维雅奖有深刻的印象。第一，施维雅奖评审很严格。记得我第一次参评顺利通过了中方评审，但是，未获法方通过，原因是与我同单位的前面获奖者当年出国留学，没有履行“获奖后一年内不长期出国”的保证。第二，施维雅奖评委很公平。虽然我第一次参评错过获奖，但是，在我再次申报时中法双方评委给予了免评通过，可见评委们充分考虑到我本人完全符合获奖条件。特别是，当我的论文获得全国优秀博士学位论文奖，更说明施维雅奖评委公平和有眼力。第三，施维雅奖很有影响力。该奖是我当年顺利晋升副教授的标志性成绩，目前仍然是我校晋升职称的重要指标(这不仅指施维雅药理学奖，也包括施维雅药物化学奖)。在中国，年轻人以获得施维雅奖为莫大光荣，将施维雅奖视为科研生涯的起飞标志。

施维雅奖之后，我的各项工作又取得重要进展。在心脑血管药理学研究方面，获得国家自然科学二等奖等多项奖励，以及国家一类新药证书等多项批文。成为国家杰出青年科学基金获得者，国家药效学平台首席专家，国家药理学精品课程负责人，全国巾帼建国标兵，全国优秀科技工作者。受聘为国家重点学科第二军医大学药理学教研室主任，当选为中国药理学会心血管药理专业委员会主任委员。期间，我培养的学生有 2 名获施维雅奖，1 名获国家优秀青年科学基金。我们师生在施维雅奖的鼓励下，不忘初心，为中国药理学事业，为中国成为创新型国家，奋发努力工作。

今天，2016 年 10 月 24 日，我们在北京庆祝中国药理学会-施维雅青年药理学工作者奖 20 周年！在这大喜日子里，再次感谢法国施维雅集团，感谢 Paul M. Vanhoutte 教授提出设立施维雅奖，谢谢你们对中国药理学工作者的莫大帮助，对中国药理学事业的贡献！

最后，衷心祝愿中国药理学会、法国施维雅集团明天更辉煌！

Merci Beaucoup!

2016 年全国心脑血管药理学术会议召开

2016 年 10 月 14-16 日，中国药理学会第十一届心血管药理专业委员会在浙江省杭州市纳德自由酒店召开“2016 年全国心脑血管药理学术会议”。本次大会由中国药理学会心血管药理专业委员会主办，第二军医大学、浙江省药理学会、浙江省药学会药理专业委员会承办。大会主题为“重大心脑血管疾病的基础及转化研究”。来自全国各地的心血管药理研究者以及研究生共计 300 余位参会者参加了此次盛会。共收到参加会议的论文摘要 135 篇，以及参加青年优秀论文评选的全文 30 余篇。

中国药理学会第十一届心血管药理专业委员会主任委员缪朝玉教授以及浙江大学基础医学院副院长陈忠教授做大会开幕式致词。哈尔滨医科大学校长/中国工程院院士杨宝峰教授、第二军医大学苏定冯教授、中山大学关永源教授、北京大学基础医学院李学军教授、第二军医大学缪朝玉教授、中国医学科学院药物研究所王晓良教授、北京大学第三医院张幼怡教授、南京医科大学季勇教授等专家做了精彩的大会报告。此外，研讨会还安排了 32 个专题报告，内容涉及心血管药理学相关研究领域的最新成果，会场学术气氛浓厚，讨论热烈，促进了学科和地区之间的交流。

Acta Pharmacologica Sinica(中国药理学报)编辑部吴民淑主任和 British Journal of Pharmacology(英国药理学杂志)副主编南京医科大学季勇教授分别就该两本药理学领域 SCI 期刊在大会上做了详细的介绍，大家受益匪浅。

本次会议还举办了青年优秀论文报告，吸引了三十多名青年药理学工作者或博士投稿参与。前期，经过会议主席第二军医大学缪朝玉教授及秘书长王培副教授等的提前筛选，共选出 12 名来自浙江大学、第二军医大学、哈尔滨医科大学、中山大学、首都医科大学、遵义医学院等院校的青年药理学工作者或博士参加最后的口头报告。经过现场 6 名评委的评选，第二军医大学张赛龙等人分获一等奖、二等奖及优胜奖，并获得相应的奖金奖励。

会议期间，还召开了专业委员会工作会议。报告了本次研讨会的筹备情况，商讨了筹办专业委员会青年委员会、拟增补委员名单，以及 2017 年会议的时间及地点。与会人员各抒己见，热烈讨论。

缪朝玉教授赴泰国参加亚太药理学家联盟大会

缪朝玉教授应邀于 2016 年 2 月 1-3 日出席在泰国曼谷召开的“第 13 届亚太药理学家联盟大会”。该会议由泰国药理和治疗学会、亚太药理学家联盟举办，主题是“为了全球健康的药理学新模式”。会议开幕式由大会主席、泰国药理和治疗学会理事长 Kesara Na-Bangchang 主持，泰国卫生部长 Piyasakol Sakolsatayadorn、亚太药理学家联盟主席 Samuel H.H. Chan 在开幕式上致辞。

在这次大会上，缪朝玉教授应邀做专题报告，题目是“脂肪因子作为血管疾病治疗的新靶点(Adipokines as novel therapeutic targets for vascular disease)”。报告获得会议主持人的赞扬，以及与会代表的兴趣、提问和讨论。

上一届会议，即“第 12 届亚太药理学家联盟大会”是 2013 年 7 月 9-13 日在上海国际会议中心召开，由亚太药理学家联盟、中国药理学会主办，第二军医大学、上海市药理学会承办。缪朝玉教授曾于 2013 年作为承办单位会议组织负责人之一，接待过来自 16 个国家和地区 1000 余名参会代表，包括来自泰国药理学会主要领导和专家。因此，这次缪朝玉教授参会从飞机降落曼谷到会议结束飞机离开曼谷，在泰国全程受到热情接待。

这次在泰国的会议很成功。中国是除主办国泰国以外，参会人数最多的国家，有 60 余人参加了会议。会议期间，我们中国药理学会的同仁在各个会场展现了中国药理学研究进展，体现了团结协作的精神风貌。除了学术报告交流，在会议组织的晚宴活动中，我们又进一步加深了与来自亚洲太平洋地区的相关学术组织领导、专家、学者的友谊。

缪朝玉教授邀请报告英文信息：Chao-Yu Miao. Adipokines as novel therapeutic targets for vascular disease. The 13th Asia Pacific Federation of Pharmacologists (APFP) Meeting “New Paradigms in Pharmacology for Global Health”. 1-3 February 2016, Bangkok, Thailand.

(下附 4 张照片)

缪朝玉教授在“第 13 届亚太药理学家联盟大会”上做学术报告

缪朝玉教授接受大会主办单位赠送的纪念品

“第 13 届亚太药理学家联盟大会”晚宴活动要求穿民族服装出席，缪朝玉教授着旗袍，牵手的是泰国药理和治疗学会理事长 Kesara Na-Bangchang 教授

参加“第 13 届亚太药理学家联盟大会”部分中国代表合影

左起：朱晓新，缪朝玉，杜冠华，陈忠

药理学课程入选首批国家级精品资源共享课

第二军医大学药理学教研室建设的药理学课程入选首批国家级精品资源共享课。该课程由缪朝玉教授担任负责人，26 名老师组成教学团队。

医学电子书包《药理学》出版

由第二军医大学药理学教研室苏定冯教授担任主编的全国高等教育医学数字化规划教材、国家医学电子书包《药理学》于 2016 年 4 月出版。

药理学

简介：

教材叙述临床用药的基本理论知识，注重与临床实践相结合，图表配合文字对照阐明问题，设置“案例分析”，“药物制剂与用法”等特色板块内容，形象、直观、立体、互动，且实践性强。教材内容强调知识的海量化、形象性、科学性、新颖性、先进性和适用性。编写力求定义准确、概念清楚、重点突出、结构严谨、层次分明、逻辑性强、语言流畅、叙述明晰。以五年制学生为主要对象，还包含有长学制扩展内容及人量的延伸内容，可供八年制学生、研究生和临床医生参考阅读。

教材正文文字96万，长学制拓展及延伸内容82万字，同步测试题近千道。近千个教学动画及视频，近千幅高清图片，4000多个交互特效。

特色:

1.药物的平面结构式与3D结构式一一对应。

2.药动学、药代学内容动画演示，生动有趣，易学好记。

编委名录

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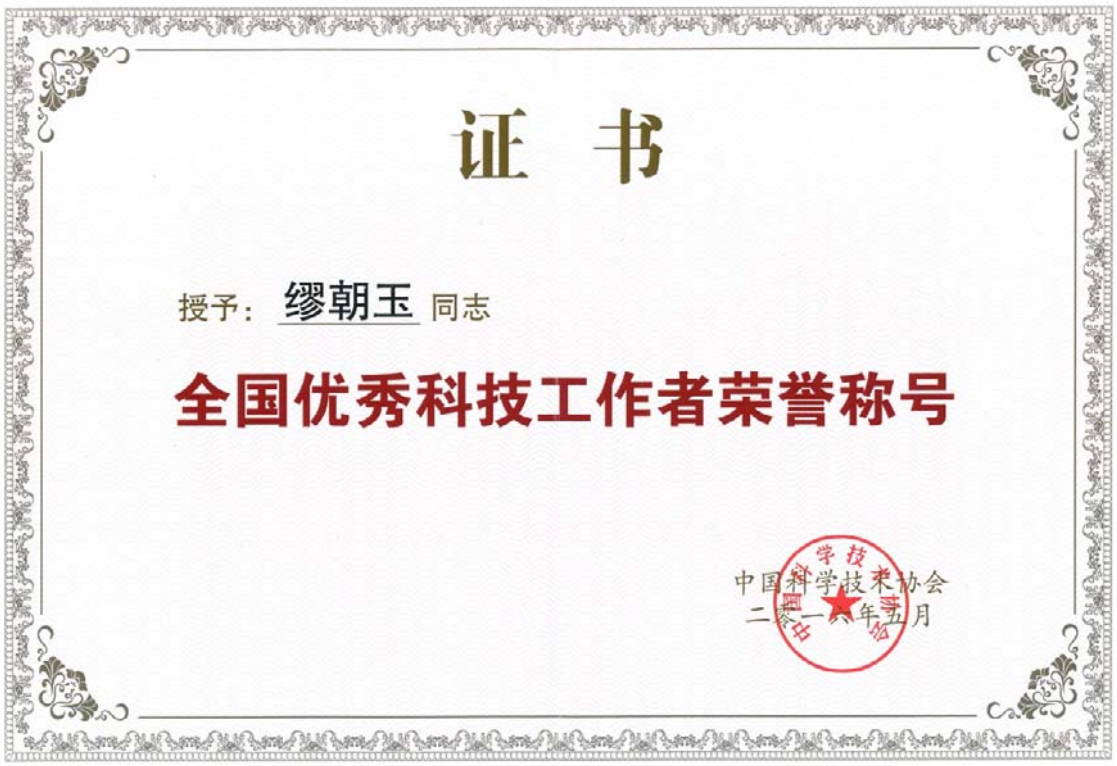
学术秘书	李 玲 第二军医大学		

人卫慕课《药理学》上线开课

中国医学教育慕课联盟组织的人卫慕课《药理学》于 2016 年 9 月上线，该课程由哈尔滨医科大学、第二军医大学、山东大学、大连医科大学 4 所大学联合制作。第二军医大学药理学教研室承担了其中 12 章 280 分钟的慕课录制任务。

缪朝玉教授获全国优秀科技工作者荣誉称号

第二军医大学药理学教研室主任缪朝玉教授获第七届全国优秀科技工作者荣誉称号。



王培副教授获上海市青年五四奖章

中国药理学会心血管药理专业委员会秘书长、第二军医大学药理学教研室副主任王培副教授获“上海市青年五四奖章”称号。

李志勇讲师获中国药理学会-施维雅青年药理学工作者奖

在 2016 年“中国药理学会第十四次全国学术大会暨中国药理学会-施维雅优秀青年药理学工作者奖 20 周年学术论坛”会议上，第二军医大学药理学教研室李志勇讲师获中国药理学会-施维雅青年药理学工作者奖。

孙旸讲师获 2016 年中国药理学会青年药理学家奖

在“中国药理学会第十四次全国学术大会暨中国药理学会-施维雅优秀青年药理学工作者奖 20 周年学术论坛”会议上，第二军医大学药理学教研室孙旸讲师获 2016 年中国药理学会青年药理学家奖。


荣誉证书

孙 旸 同志：

荣获“2016年中国药理学会青年药理学家奖”。

特发此奖，以示鼓励。

中国药理学会理事长 2016年10月24日

中国药理学会 2016年10月24日

第二军医大学药理学教研室 2016 年 SCI 论文(摘要刊登)

1. Sun Y, Yang YL, Qin Z, Cai JY, Guo XM, Tang Y, Wan JJ, Su DF, Liu X. The acute-phase protein orosomucoid regulates food intake and energy homeostasis via leptin receptor signaling pathway. Diabetes 2016;65(6):1630-41.

Abstract:

The acute-phase protein orosomucoid (ORM) exhibits a variety of activities in vitro and in vivo, notably modulation of immunity and transportation of drugs. We found in this study that mice lacking ORM1 displayed aberrant energy homeostasis characterized by increased body weight and fat mass. Further investigation found that ORM, predominantly ORM1, is significantly elevated in sera, liver, and adipose tissues from the mice with high-fat diet (HFD)– induced obesity and db/db mice that develop obesity spontaneously due to mutation in the leptin receptor (LepR). Intravenous or intraperitoneal administration of exogenous ORM decreased food intake in C57BL/6, HFD, and leptin-deficient ob/ob mice, which was absent in db/db mice and was significantly reduced in mice with arcuate nucleus (ARC) LepR knockdown, whereas enforced expression of ORM1 in ARC significantly decreased food intake, body weight, and serum insulin level. Furthermore, we found that ORM is able to bind directly to LepR and activate the receptor-mediated JAK2–STAT3 signaling in hypothalamus tissue and GT1-7 cells, which was derived from hypothalamic tumor. These data indicated that ORM could function through LepR to regulate food intake and energy homeostasis in response to nutrition status. Modulating the expression of ORM is a novel strategy for the management of obesity and related metabolic disorders.

2. Zhou CC, Yang X, Hua X, Liu J, Fan MB, Li GQ, Song J, Xu TY, Li ZY, Guan YF, Wang P, Miao CY. Hepatic NAD(+) deficiency as a therapeutic target for non-alcoholic fatty liver disease in ageing. Br J Pharmacol 2016;173(15):2352-68.

Abstract:

BACKGROUND AND PURPOSE: Ageing is an important risk factor of non-alcoholic fatty liver disease (NAFLD). Here, we investigated whether the deficiency of nicotinamide adenine dinucleotide (NAD(+)), a ubiquitous coenzyme, links ageing with NAFLD. EXPERIMENTAL APPROACH: Hepatic concentrations of NAD(+), protein levels of nicotinamide phosphoribosyltransferase (NAMPT) and several other critical enzymes regulating NAD(+) biosynthesis, were compared in middle-aged and aged mice or patients. The influences of NAD(+) decline on the steatosis and steatohepatitis were evaluated in wild-type and H247A dominant-negative, enzymically-inactive NAMPT transgenic mice (DN-NAMPT) given normal or high-fat diet (HFD). KEY RESULTS: Hepatic NAD(+) level decreased in aged mice and humans. NAMPT-controlled NAD(+) salvage, but not de novo biosynthesis pathway, was compromised in liver of elderly mice and humans. Given normal chow, middle-age DN-NAMPT mice displayed systemic NAD(+) reduction and had moderate NAFLD phenotypes, including lipid accumulation, enhanced oxidative stress, triggered inflammation and impaired insulin sensitivity in liver. All these NAFLD phenotypes, especially release of pro-inflammatory factors, Kupffer cell accumulation, monocytes infiltration, NLRP3 inflammasome pathway and hepatic fibrosis (Masson's staining and alpha-SMA staining), deteriorated further under HFD challenge. Oral

administration of nicotinamide riboside, a natural NAD(+) precursor, completely corrected these NAFLD phenotypes induced by NAD(+) deficiency alone or HFD, whereas adenovirus-mediated SIRT1 overexpression only partially rescued these phenotypes. CONCLUSIONS AND IMPLICATIONS: These results provide the first evidence that ageing-associated NAD(+) deficiency is a critical risk factor for NAFLD, and suggest that supplementation with NAD(+) substrates may be a promising therapeutic strategy to prevent and treat NAFLD.

3. Qin Z, Wang PY, Su DF, Liu X. miRNA-124 in immune system and immune disorders. Front Immunol 2016;7:406.

Abstract:

In recent years, miR-124 has emerged as a critical modulator of immunity and inflammation. Here, we summarize studies on the function and mechanism of miR-124 in the immune system and immunity-related diseases. They indicated that miR-124 exerts a crucial role in the development of immune system, regulation of immune responses, and inflammatory disorders. It is evident that miR-124 may serve as an informative diagnostic biomarker and therapeutic target in the future.

4. Lei H, Sun Y, Luo Z, Yourek G, Gui H, Yang Y, Su DF, Liu X. Fatigue-induced orosomucoid 1 acts on C-C chemokine receptor type 5 to enhance muscle endurance. Sci Rep 2016;6:18839.

Abstract:

Understanding and managing fatigue is a significant challenge in clinic and society. In attempting to explore how the body responds to and regulates fatigue, we found in rodent fatigue models that orosomucoid 1 (ORM1) was significantly increased in multiple tissues, including blood and muscle. Interestingly, administration of exogenous ORM1 increased muscle glycogen and enhanced muscle endurance, whereas ORM1 deficiency resulted in a significant decrease of muscle endurance both in vivo and in vitro, which could largely be restored by exogenous ORM1. Further studies demonstrated that ORM1 can bind to C-C chemokine receptor type 5 (CCR5) on muscle cells and deletion of the receptor abolished the effect of ORM1. Thus, fatigue upregulates the level of ORM1, which in turn functions as an anti-fatigue protein to enhance muscle endurance via the CCR5 pathway. Modulation of the level of ORM1 and CCR5 signaling could be a novel strategy for the management of fatigue.

5. Xu ZQ, Shao BZ, Ke P, Liu JG, Liu GK, Chen XW, Su DF, Liu C. Combined administration of anisodamine and neostigmine rescued acute lethal crush syndrome through α7nAChR-dependent JAK2-STAT3 signaling. Sci Rep 2016;6:37709.

Abstract:

Previously we showed that Ani (anisodamine)/Neo (neostigmine) combination produced anti-shock effect via activating α7 nicotinic acetylcholine receptor (α7nAChR). In this study, we aim to investigate the therapeutic effect and underlying mechanisms of Ani/Neo combination in acute lethal crush syndrome (CS). In rat and rabbit CS models, Ani/Neo combination increased the 24 h survival rates, improved hemodynamics and decreased the levels of creatine kinase, MB isoenzyme of creatine kinase, blood urea nitrogen, creatinine, K+ in serum. It also decreased the levels of H2O2, myeloperoxidase (MPO) and nitric oxide (NO) in serum and compressed muscle in rat CS model. In wild-type (WT) mice with CS, Ani/Neo combination increased 24 h survival

rate and decreased the levels of H2O2, MPO, NO, TNFα, IL-6 and IL-10 in compressed muscle. These effects were attenuated by α7nAChR knockout (KO). Moreover, Ani/Neo combination prevented the decrease of phosphorylation of Janus kinase 2 (JAK2) and phosphorylation of signal transducer and activator of transcription 3 (STAT3) induced by CS. These effects of Ani/Neo in CS mice were cancelled by methyllycaconitine (α7nAChR antagonist) and α7nAChR KO. Collectively, our results demonstrate that Ani/Neo combination could produce therapeutic effects in CS. The underlying mechanism involves the activation of α7nAChR-dependent JAK2-STAT3 signaling pathway.

6. Wang P, Yang X, Zhang Z, Song J, Guan YF, Zou DJ, Miao CY. Depletion of NAD pool contributes to impairment of endothelial progenitor cell mobilization in diabetes. Metabolism 2016;65(6):852-62.

Abstract:

OBJECTIVE: The impaired mobilization of endothelial progenitor cells (EPCs) from bone marrow (BM) critically contributes to the diabetes-associated vascular complications. Here, we investigated the relationship between the nicotinamide phosphoribosyltransferase (NAMPT)-controlled nicotinamide adenine dinucleotide (NAD) metabolism and the impaired mobilization of BM-derived EPCs in diabetic condition. METHODS: The NAMPT-NAD pool in BM and BM-derived EPCs in wild-type (WT) and diabetic db/db mice was determined. Nicotinamide, a natural substrate for NAD biosynthesis, was administrated for 2weeks in db/db mice to examine the influence of enhancing NAD pool on BM and blood EPCs number. The modulations of stromal cell-derived factor-1alpha (SDF-1alpha) and endothelial nitric oxide synthase (eNOS) protein in BM were measured using immunoblotting. The EPCs intracellular NAMPT level and NAD concentration, as well as the blood EPCs number, were compared between 9 healthy people and 16 patients with type 2 diabetes mellitus (T2DM). The T2DM patients were treated with nicotinamide for two weeks and then the blood EPCs number was determined. Moreover, the association between blood EPCs numbers and EPCs intracellular NAD(+)/NAMPT protein levels in 21 healthy individuals was determined. RESULTS: We found that NAD concentration and NAMPT expression in BM and BM-derived EPCs of db/db mice were significantly lower than those in WT mice BM. Enhancing NAD pool not only increased the EPCs intracellular NAD concentration and blood EPCs number, but also improved post-ischemic wound healing and blood reperfusion in db/db mice with hind-limb ischemia model. Enhancing NAD pool rescued the impaired modulations of stromal cell-derived factor-1alpha (SDF-1alpha) and endothelial nitric oxide synthase (eNOS) protein levels in db/db mice BM upon hind-limb ischemia. In addition, enhancing NAD pool significantly inhibited PARP and caspase-3 activates in db/db mice BM. The intracellular NAMPT-NAD pool was positively associated with blood EPCs number in healthy individuals. At last, we found that the EPC intracellular NAMPT and NAD(+) levels were reduced in T2DM patients and enhancing NAD pool elevated the circulating blood EPCs number in T2DM patients. CONCLUSION: Our results indicate that the depletion of NAD pool may contribute to the impairment of EPCs mobilization in diabetic condition, and imply the potential therapeutic value of nicotinamide in the prevention and treatment for cardiovascular complications of diabetes.

7. Qin Z, Wan JJ, Sun Y, Wang PY, Su DF, Lei H, Liu X. ORM Promotes Skeletal Muscle

Glycogen Accumulation via CCR5-Activated AMPK Pathway in Mice. Front Pharmacol 2016;7:302.

Abstract:

We found previously that acute phase protein orosomucoid reacts to fatigue and activates C-C chemokine receptor type 5 to increase muscle glycogen storage and enhance muscle endurance (Leietal.,2016). To explore the underlying molecular mechanisms, we investigated the role of AMP-activated protein kinase, a critical fuel sensor in skeletal muscle, in C-C chemokine receptor type 5-mediated orosomucoid action. It was found orosomucoid increased skeletal muscle AMP-activated protein kinase activation in a time- and dose-dependent manner, which was largely prevented by pharmacological blocking or knockout of C-C chemokine receptor type 5. Administration of orosomucoid also significantly increased the de-phosphorylation and activity of muscle glycogen synthase, the rate-limiting enzyme for glycogen synthesis. The effect was largely absent in mice deficient in C-C chemokine receptor type 5 −/− or AMP-activated protein kinase a2 −/−, the predominant isoform in skeletal muscle. Moreover, deletion of AMP-activated protein kinase a2 abolished the effect of or osomucoid on fatigue and muscle glycogen. These findings indicate that orosomucoid may promote glycogen storage and enhance muscle function through C-C chemokine receptor type 5-mdiated activation of AMP-activated protein kinase, which in turn activates glycogen synthase and increases muscle glycogen.

8. Fan B, Zhang EH, Wu M, Guo JM, Su DF, Liu X, Yu JG. Activation of α7 nicotinic acetylcholine receptor decreases on-site mortality in crush syndrome through insulin signaling-Na/K-ATPase pathway. Front Pharmacol 2016;7:79.

Abstract:

On-site mortality in crush syndrome remains high due to lack of effective drugs based on definite diagnosis. Anisodamine (Ani) is widely used in China for treatment of shock, and activation of a7 nicotinic acetylcholine receptor (a7nAChR) mediates such antishock effect. The present work was designed to test whether activation of a7nAChR with Ani decreased mortality in crush syndrome shortly after decompression. Sprague-Dawley rats and C57BL/6 mice with crush syndrome were injected with Ani (20 mg/kg and 28 mg/kg respectively, i.p.) 30 min before decompression. Survival time, serum potassium, insulin, and glucose levels were observed shortly after decompression. Involvement of a7nAChR was verified with methyllycaconitine (selective a7nAChR antagonist) and PNU282987 (selective a7nAChR agonist), or in a7nAChR knockout mice. Effect of Ani was also appraised in C2C12 myotubes. Ani reduced mortality and serum potassium and enhanced insulin sensitivity shortly after decompression in animals with crush syndrome, and PNU282987 exerted similar effects. Such effects were counteracted by methyllycaconitine or in a7nAChR knockout mice. Mortality and serum potassium in rats with hyperkalemia were also reduced by Ani. Phosphorylation of Na/K-ATPase was enhanced by Ani in C2C12 myotubes. Inhibition of tyrosine kinase on insulin receptor, phosphoinositide 3-kinase, mammalian target of rapamycin, signal transducer and activator of transcription 3, and Na/K-ATPase counteracted the effect of Ani on extracellular potassium. These findings demonstrated that activation of a7nAChR could decrease on-site mortality in crush syndrome, at least in part based on the decline of serum potassium through insulin signaling-Na/K-ATPase pathway.

9. Fan BS, Zhang EH, Cheng MH, Wu ZT, Han B, Yu JG. Diurnal variation of the peripheral cholinergic antiinflammatory function in mice. CNS Neurosci Ther 2016; 22(9):764-70.

Abstract:

Aims: Cholinergic antiinflammatory (CAI) pathway functions importantly in inflammation via a7 nicotinic acetylcholine receptors (a7nAChR). The present work tested circadian rhythm in peripheral CAI activity and validities of CAI activity and glucocorticoids in chronotherapy for lipopolysaccharide (LPS)-induced shock. Methods: Vesicular acetylcholine transporter (VAChT) expressed in liver and kidney was examined every 3 h in C57BL/6 mice. Proinflammatory cytokines in serum and survival time in shock were monitored after LPS injection every 3 h. Mifepristone, antagonist of glucocorticoid receptors, and methyllycaconitine (MLA), antagonist of a7nAChR, were administrated before LPS to block antiinflammatory function of endogenous glucocorticoids and acetylcholine. Results: Both levels of tumor necrosis factor a, interleukin 1b, and interleukin 6 and mortality exhibited diurnal variations with prominent peaks when LPS was given at 15:00, and the minimum mortality occurred at 00:00. Expression of VAChT increased during resting period. MLA increased serum proinflammatory cytokines slightly, but not affected survival rate. Both differences in cytokines and in survival times between LPS injection at 15:00 and 00:00 were eliminated by mifepristone, but not by MLA. Conclusion: Peripheral CAI pathway exerts more powerful antiinflammatory effect during resting period. Glucocorticoids appear to be efficient in chronotherapy for septic shock.

10. Zhang LL, Liu HQ,Yu XH, Zhang Y, Tian JS, Song XR, Han B, Liu AJ. The combination of scopolamine and psychostimulants for the prevention of severe motion sickness. CNS Neurosci Ther 2016;22(8):715–22.

Abstract:

Summary Background and aims Severe motion sickness is a huge obstacle for people conducting precise aviation, marine or emergency service tasks. The combination of scopolamine and d -amphetamine is most effective in preventing severe motion sickness. However, this combination is not included in any present pharmacopoeia due to the abuse liability of d -amphetamine. We wanted to find a combination to replace it for the treatment of severe motion sickness. Methods and results We compared the efficacy of scopolamine, diphenhydramine, and granisetron (representing three classes of drugs) with different doses, and found that scopolamine was the most effective one. We also found scopolamine inhibited central nervous system at therapeutic doses and caused anxiety. Then, we combined it with different doses of psychostimulants (d -amphetamine, modafinil, caffeine) to find the best combination for motion sickness. The efficacy of scopolamine with modafinil (1 + 10 mg/kg) was equivalent to that of scopolamine with d -amphetamine (1 + 1 mg/kg); This combination also excited central nervous system and abolished the anxiety caused by scopolamine. Conclusions The optimal dose ratio of scopolamine and modafinil is 1:10. This combination is beneficial for motion sickness and can abolish the side effects of scopolamine. So, it might be a good replacement of scopolamine and d -amphetamine for severe motion sickness.

11. Liu Y, Jiang S, Yang PY, Zhang YF, Li TJ, Rui YC. EF1A1/HSC70 cooperatively suppress brain endothelial cell apoptosis via regulating JNK activity. CNS Neurosci Ther

2016;22(10):836-44.

Abstract

AIMS:

In our previous study, eEF1A1 was identified to be a new target for protecting brain ischemia injury, but the mechanism remains largely unknown. In this study, we screened the downstream cellular protein molecules interacted with eEF1A1 and found mechanism of eEF1A1 in brain ischemia protection.

METHODS AND RESULTS:

Through co-immunoprecipitation and mass spectrometry for searching the interaction of proteins with eEF1A1 in bEnd3 cells, HSC70 was identified to be a binding protein of eEF1A1, which was further validated by Western blot and immunofluorescence. eEF1A1 or HSC70 knockdown, respectively, increased OGD-induced apoptosis of brain vascular endothelial cells, which was detected by Annexin V-FITC/PI staining. HSC70 or eEF1A1 knockdown enhances phosphorylated JNK, phosphorylation of c-JUN (Ser63, Ser73), cleaved caspase-9, and cleaved caspase-3 expression, which could be rescued by JNK inhibitor.

CONCLUSION:

In summary, our data suggest that the presence of chaperone forms of interaction between eEF1A1 and HSC70 in brain vascular endothelial cells, eEF1A1 and HSC70 can play a protective role in the process of ischemic stroke by inhibiting the JNK signaling pathway activation.

12. Wang SN, Xu TY, Li WL, Miao CY. Targeting nicotinamide phosphoribosyltransferase as a potential therapeutic strategy to restore adult neurogenesis. CNS Neurosci Ther 2016;22(6):431-9.

Abstract:

Adult neurogenesis is the process of generating new neurons throughout life in the olfactory bulb and hippocampus of most mammalian species, which is closely related to aging and disease. Nicotinamide phosphoribosyltransferase (NAMPT), also an adipokine known as visfatin, is the rate-limiting enzyme for mammalian nicotinamide adenine dinucleotide (NAD) salvage synthesis by generating nicotinamide mononucleotide (NMN) from nicotinamide. Recent findings from our laboratory and other laboratories have provided much evidence that NAMPT might serve as a therapeutic target to restore adult neurogenesis. NAMPT-mediated NAD biosynthesis in neural stem/progenitor cells is important for their proliferation, self-renewal, and formation of oligodendrocytes in vivo and in vitro. Therapeutic interventions by the administration of NMN, NAD, or recombinant NAMPT are effective for restoring adult neurogenesis in several neurological diseases. We summarize adult neurogenesis in aging, ischemic stroke, traumatic brain injury, and neurodegenerative disease and review the advances of targeting NAMPT in restoring neurogenesis. Specifically, we provide emphasis on the P7C3 family, a class of proneurogenic compounds that are potential NAMPT activators, which might shed light on future drug development in neurogenesis restoration.

13. Wang SN, Xu TY, Wang X, Guan YF, Zhang SL, Wang P, Miao CY. Neuroprotective efficacy of an aminopropyl carbazole derivative p7c3-a20 in ischemic stroke. CNS Neurosci Ther 2016;22(9):782-8.

Abstract:

AIM: NAMPT is a novel therapeutic target of ischemic stroke. The aim of this study was to investigate the effect of a potential NAMPT activator, P7C3-A20, an aminopropylcarbazole derivative, on ischemic stroke. METHODS: In vitro study, neuron protection effect of P7C3-A20 was investigated by co-incubation with primary neurons subjected to oxygen-glucose deprivation (OGD) or oxygen-glucose deprivation/reperfusion (OGD/R) injury. In vivo experiment, P7C3-A20 was administrated in middle cerebral artery occlusion (MCAO) rats and infarct volume was examined. Lastly, the brain tissue nicotinamide adenine dinucleotide (NAD) levels were detected in P7C3-A20 treated normal or MCAO mice. RESULTS: Cell viability, morphology, and Tuj-1 staining confirmed the neuroprotective effect of P7C3-A20 in OGD or OGD/R model. P7C3-A20 administration significantly reduced cerebral infarction in MCAO rats. Moreover, brain NAD levels were elevated both in normal and MCAO mice after P7C3-A20 treatment. CONCLUSIONS: P7C3-A20 has neuroprotective effect in cerebral ischemia. The study contributes to the development of NAMPT activators against ischemic stroke and expands the horizon of the neuroprotective effect of aminopropylcarbazole chemicals.

14. Shi HQ, Zhang Y, Cheng MH, Fan BS, Tian JS, Yu JG, Chen B. Sodium sulfide, a hydrogen sulfide-releasing molecule, attenuates acute cerebral ischemia in rats. CNS Neurosci Ther 2016; 22(7):625-32.

Abstract:

Abstract Aims: Acute cerebral ischemia may lead to ischemic stroke, which is a major cause of death and disability worldwide. Hydrogen sulfide (H2 S) functions importantly in mammalian systems. The present work was designed to study the effect of sodium sulfide, a donor of H2 S, on acute cerebral ischemia. Methods: Acute cerebral focal ischemia was produced by middle cerebral artery occlusion (MCAO) in Sprague-Dawley (SD) rats. Bilateral vertebral arteries and common carotid arteries were blocked to establish cerebral global ischemia in SD rats. Acute cerebral anoxia was produced by hypobaric anoxia in C57BL/6 mice and hypoxic anoxia in SD rats. Nimodipine and aspirin were set as positive control separately. Results: Infarct size after MCAO was decreased by sodium sulfide. Sodium sulfide improved cerebral energy metabolism after cerebral global ischemia and prolonged survival time of animals with acute cerebral anoxia. In addition, increased cerebral blood flow and decreased cerebrovascular resistance, blood viscosity, and thrombogenesis were observed in animals treated with sodium sulfide. In cultured neurons, sodium sulfide increased cell viability and decreased cell apoptosis induced by oxygen-glucose deprivation. Conclusion: Sodium sulfide, a H2S donor, presents protective effect on acute cerebral ischemia, and might be a promising therapeutic drug.

15. Ke P, Shao BZ, Xu ZQ, Wei W, Han BZ, Chen XW, Su DF, Liu C. Activation of cannabinoid receptor 2 ameliorates DSS-induced colitis through inhibiting NLRP3 inflammasome in macrophages. PLoS One 2016;11(9):e0155076.

Abstract:

Activation of cannabinoid receptor 2 (CB2R) ameliorates inflammation, but the underlying mechanism remains unclear. In the present study, we examined whether activation of CB2R could suppress the nucleotide-binding domain and leucine-rich repeat protein 3 (NLRP3) inflammasome. In peritoneal macrophages isolated from C57BL/6 mice, LPS/ DSS challenge for 24 h increased the expression of the components of NLRP3 inflammasome NLRP3, Casp-1 p20/Casp-1 p45 ratio,

proIL-1β and IL-1β and also enhanced autophagy (LC3-II/LC3-I ratio, Beclin-1 and SQSTM1). Pretreatment of peritoneal macrophages with HU 308, a selective CB2R agonist, attenuated LPS/DSS-induced NLRP3 inflammasome activation, but further enhanced autophagy. In comparison with wild-type (WT) control, peritoneal macrophages from CB2R knockout (KO) mice had more robust NLRP3 inflammasome activation and attenuated autophagy upon LPS/DSS challenge. Knockdown autophagy-related gene 5 (Atg5) with a siRNA in peritoneal macrophages attenuated the inhibitory effects of HU 308 on LPS/DSS-induced NLRP3 inflammasome activation in vitro. In vivo, HU308 treatment attenuated DSS-induced colitis mice associated with reduced colon inflammation and inhibited NLRP3 inflammasome activation in wild-type mice. In CB2R KO mice, DSS-induced inflammation and NLRP3 inflammasome activation were more pronounced than those in WT control. Finally, we demonstrated that AMPK-mTORP70S6K signaling pathway was involved in this CB2R-mediated process.We conclude that activation of CB2R ameliorates DSS-induced colitis through enhancing autophagy that may inhibit NLRP3 inflammasome activation in macrophages.

16. Zhu Q, Zhang Y, Liu Y, Cheng H, Wang J, Zhang Y, Rui Y, Li T. MLIF alleviates SH-SY5Y neuroblastoma injury induced by oxygen-glucose deprivation by targeting eukaryotic translation elongation factor 1A2. PLoS One 2016;11(2):e0149965.

Abstract:

Monocyte locomotion inhibitory factor (MLIF), a heat-stable pentapeptide, has been shown to exert potent anti-inflammatory effects in ischemic brain injury. In this study, we investigated the neuroprotective action of MLIF against oxygen-glucose deprivation (OGD)-induced injury in human neuroblastoma SH-SY5Y cells. MTT assay was used to assess cell viability, and flow cytometry assay and Hoechst staining were used to evaluate apoptosis. LDH assay was used to exam necrosis. The release of inflammatory cytokines was detected by ELISA. Levels of the apoptosis associated proteins were measured by western blot analysis. To identify the protein target of MLIF, pull-down assay and mass spectrometry were performed. We observed that MLIF enhanced cell survival and inhibited apoptosis and necrosis by inhibiting p-JNK, p53, c-caspase9 and c-caspase3 expression. In the microglia, OGD-induced secretion of inflammatory cytokines was markedly reduced in the presence of MLIF. Furthermore, we found that eukaryotic translation elongation factor 1A2 (eEF1A2) is a downstream target of MLIF. Knockdown eEF1A2 using short interfering RNA (siRNA) almost completely abrogated the anti-apoptotic effect of MLIF in SH-SY5Y cells subjected to OGD, with an associated decrease in cell survival and an increase in expression of p-JNK and p53. These results indicate that MLIF ameliorates OGD-induced SH-SY5Y neuroblastoma injury by inhibiting the p-JNK/p53 apoptotic signaling pathway via eEF1A2. Our findings suggest that eEF1A2 may be a new therapeutic target for ischemic brain injury.

17. Shao BZ, Han BZ, Zeng YX, Su DF, Liu C. The roles of macrophage autophagy in atherosclerosis. Acta Pharmacol Sin 2016; 37(2):150-6.

Abstract:

Although various types of drugs and therapies are available to treat atherosclerosis, it remains a major cause of mortality throughout the world. Macrophages are the major source of foam cells, which are hallmarks of atherosclerotic lesions. Consequently, the roles of macrophages in the

pathophysiology of atherosclerosis are increasingly investigated. Autophagy is a self-protecting cellular catabolic pathway. Since its discovery, autophagy has been found to be associated with a variety of diseases, including cardiovascular diseases, malignant tumors, neurodegenerative diseases, and immune system disorders. Accumulating evidence demonstrates that autophagy plays an important role in inhibiting inflammation and apoptosis, and in promoting efferocytosis and cholesterol efflux. These facts suggest the induction of autophagy may be exploited as a potential strategy for the treatment of atherosclerosis. In this review we mainly discuss the relationship between macrophage autophagy and atherosclerosis and the molecular mechanisms, as well as the recent advances in targeting the process of autophagy to treat atherosclerosis.

18. Li ZY, Fan MB, Zhang SL, Qu Y, Zheng SL, Song J, Miao CY. Intestinal Metrnl released into the gut lumen acts as a local regulator for gut antimicrobial peptides. Acta Pharmacol Sin 2016;37(11):1458-66.

Abstract:

AIM: Metrnl is a novel secreted protein, but its physiological roles remain elusive. In this study, we investigated the tissue expression pattern of Metrnl in humans and explored its possible physiological role in the tissues with most highly expressed levels. METHODS: A human tissue microarray containing 19 types of tissues from 69 donors was used to examine the tissue expression pattern of Metrnl, and the expression pattern was further verified in fresh human and mouse tissues. Intestinal epithelial cell-specific Metrnl knockout mice were generated, which were used to analyze the physiological roles of Metrnl. RESULTS: Metrnl was the most highly expressed in the human gastrointestinal tract, and was specifically expressed in the intestinal epithelium. Consistent with this, Metrnl mRNA was also most highly expressed in the mouse gastrointestinal tract among the 14 types of tissues tested. In the intestinal epithelial cell-specific Metrnl knockout mice, the Metrnl levels in the gut fluid were significantly reduced, whereas the Metrnl serum levels showed a trend towards a reduction, but this change was not statistically significant. This cell-specific deletion of Metrnl did not affect body weight, food intake, blood glucose, colon length and histology, intestinal permeability, mucus content or mucin 2 expression under physiological conditions, but statistically decreased the expression of antimicrobial peptides, such as regenerating islet-derived 3 gamma (Reg3g) and lactotransferrin. CONCLUSION: Metrnl is highly expressed in the intestinal epithelial cells of humans and mice, which mainly contributes to the local gut Metrnl levels and affects the serum Metrnl level to a lesser extent. Metrnl plays a role in maintaining gut antimicrobial peptides.

19. Sun Y, Qin Z, Li Q, Wan JJ, Cheng MH, Wang PY, Su DF, Yu JG, Liu X. MicroRNA-124 negatively regulates LPS-induced TNF-α production in mouse macrophages by decreasing protein stability. Acta Pharmacol Sin 2016; 37(7):889-97.

Abstract:

Aim: MicroRNAs play pivotal roles in regulation of both innate and adaptive immune responses. In the present study, we investigated the effects of microRNA-124 (miR-124) on production of the pro-inflammatory cytokine TNF-α in lipopolysaccharide (LPS)-treated mouse macrophages.

Methods: Mouse macrophage cell line RAW264.7 was stimulated with LPS (100 ng/mL). The levels of miR-124 and TNF-α mRNA were evaluated using q-PCR. ELISA and Western blotting were used to detect TNF-α protein level in cell supernatants and cells, respectively. 3′-UTR

luciferase reporter assays were used to analyze the targets of miR-124. For in vivo experiments, mice were injected with LPS (30 mg/kg, ip).
Results: LPS stimulation significantly increased the mRNA level of miR-124 in RAW264.7 macrophages in vitro and mice in vivo. In RAW264.7 macrophages, knockdown of miR-124 with miR-124 inhibitor dose-dependently increased LPS-stimulated production of TNF-α protein and prolonged the half-life of TNF-α protein, but did not change TNF-α mRNA levels, whereas overexpression of miR- 124 with miR-124 mimic produced the opposite effects. Furthermore, miR-124 was found to directly target two components of deubiquitinating enzymes: ubiquitin-specific proteases (USP) 2 and 14. Knockdown of USP2 or USP14 accelerated protein degradation of TNF-α, and abolished the effect of miR-124 on TNF-α protein stability.
Conclusion: miR-124, targeting USP2 and USP14, negatively regulates LPS-induced TNF-α production in mouse macrophages, suggesting miR-124 as a new therapeutic target in inflammation-related diseases.

20. Zheng SL, Li ZY, Song J, Liu JM, Miao CY. Metrnl: a secreted protein with new emerging functions. Acta Pharmacol Sin 2016;37(5):571-9.
Abstract:
Secreted proteins play critical roles in physiological and pathological processes and can be used as biomarkers and therapies for aging and disease. Metrnl is a novel secreted protein homologous to the neurotrophinMetrn. But this protein, unlike Metrn that is mainly expressed in the brain, shows a relatively wider distribution in the body with high levels of expression in white adipose tissue and barrier tissues. This protein plays important roles in neural development, white adipose browning and insulin sensitization. Based on its expression and distinct functions, this protein is also called Cometin, Subfatin and Interleukin 39, which refer to its neurotrophic effect, adipokine function and the possible action as a cytokine, respectively. The spectrum of Metrnl functions remains to be determined, and the mechanisms of Metrnl action need to be elucidated. In this review, we focus on the discovery, structural characteristics, expression pattern and physiological functions of Metrnl, which will assist in developing this protein as a new therapeutic target or agent.

21. Jiang S, Liu Y, Wang J, Zhang Y, Rui Y, Zhang Y, Li T. Cardioprotective effects of monocyte locomotion inhibitory factor on myocardial ischemic injury by targeting vimentin. Life Sci 2016;167:85-91.
Abstract:
Monocyte locomotion inhibitory factor (MLIF), a heat-stable pentapeptide produced by Entamoeba histolytica, has anti-inflammatory function and protective effect on ischemic stroke. In this study, we evaluated the effect of MLIF on myocardial ischemia. Mice were subjected to ischemia/reperfusion by occlusion of the left anterior descending artery (LAD). After sacrifice, the serum concentrations of cardiac troponin I (cTnI), creatine kinase (CK), lactate dehydrogenase (LDH) as well as the heart infarct size were measured. HE and TUNEL staining were used to observe the pathological damage and the apoptotic cells. For in vitro study, the oxygen-glucose deprivation(OGD) model was established in H9c2 cells. MTT assay and flow cytometry assay were performed to evaluate cell viability and apoptosis. The expression of JNK and caspase 3 was assessed by western blot analysis. Pull-down assay was used to detect the specific binding protein

of MLIF in myocardial cells. MLIF significantly reduced the infarct size, and the cTnI, CK and LDH levels, ameliorated pathological damage and reduced the apopotosis compared with the myocardial I/R model group. MLIF improved cell survival and inhibited apoptosis and necrosis by inhibiting the p-JNK and cleaved caspase3 expression. Furthermore, the binding protein of MLIF in myocardial cells was vimentin. Inhibition of vimentin expression by withaferin A or vimentin siRNA repressed the protective effects of MLIF in OGD-provoked H9c2 cells. Taken together, our results demonstrate that the cardioprotective effects of MLIF on myocardial ischemia injury are related to reductions in the inflammatory response and apoptosis by targeting vimentin.

22. Chen L, Liu DH, Zhang X, Zhang EH, Liu C, Su DF, Cai GJ. Baroreflex deficiency aggravates atherosclerosis via α7 nicotinic acetylcholine receptor in mice. Vasc Pharmacol 2016; 87:92-9.

Abstract:

Objective: Inflammation and oxidative stress play a key role in the initiation, propagation, and development of atherosclerosis. Arterial baroreflex (ABR) dysfunction induced by sinoaortic denervation (SAD) promoted the development of atherosclerosis in ApoE−/− mice. The present work was designed to examine whether ABR deficiency affected inflammation and oxidative stress via α7 nicotinic acetylcholine receptor (α7nAChR) leading to the aggravation of atherosclerosis in mice.

Methods and results: ApoE−/− mice were fed with a high-cholesterol diet for 6 weeks and half of the mice received sinoaortic denervation that destroyed ABR. We studied the expression of vesicular acetylcholine transporter (VAChT), α7nAChR and levels of inflammatory response and oxidative stress. The results showed that baroreflex dysfunction could promote atherosclerosis, meanwhile, decrease the expression of VAChT and α7nAChR and significantly increase the levels of oxidative stress and inflammation in SAD mice. After treated with PNU-282987 (a selective α7nAChR agonist, 0.53 mg/kg/day) for 6 weeks in SAD and Sham mice, we found that PNU-282987 could attenuate atherosclerosis and significantly decreased oxidative stress and inflammation after SAD. In addition, α7nAChR+/+ and α7nAChR−/− mice fed with a high-cholesterol diet for 8 weeks were co-treated with ketanserin (0.6 mg/kg/day), a drug that can enhance baroreflex sensitivity (BRS). Ketanserin could alleviate atherosclerosis and markedly decrease oxidative stress and inflammation in α7nAChR+/+ mice. But there were no effects in α7nAChR knockout mice.

Conclusions: Our results demonstrate that ABR dysfunction aggravates atherosclerosis in mice via the vagus-ACh-α7nAChR-inflammation and oxidative stress pathway.

23. Wang P, Li WL, Liu JM, Miao CY. NAMPT and NAMPT-controlled NAD Metabolism in Vascular Repair. J Cardiovasc Pharmcol 2016;67(6):474-81.

Abstract:

Vascular repair plays important roles in postischemic remodeling and rehabilitation in cardiovascular and cerebrovascular disease, such as stroke and myocardial infarction. Nicotinamide adenine dinucleotide (NAD), a well-known coenzyme involved in electron transport chain for generation of adenosine triphosphate, has emerged as an important controller regulating various biological signaling pathways. Nicotinamide phosphoribosyltransferase (NAMPT) is the rate-limiting enzyme for NAD biosynthesis in mammals. NAMPT may also act in a nonenzymatic

manner, presumably mediated by unknown receptor(s). Rapidly accumulating data in the past decade show that NAMPT and NAMPT-controlled NAD metabolism regulate fundamental biological functions in endothelial cells, vascular smooth muscle cells, and endothelial progenitor cells. The NAD-consuming proteins, including sirtuins, poly-ADP-ribose polymerases (PARPs), and CD38, may contribute to the regulatory effects of NAMPT-NAD axis in these cells and vascular repair. This review discusses the current data regarding NAMPT and NAMPT-controlled NAD metabolism in vascular repair and the clinical potential translational application of NAMPT-related products in treatment of cardiovascular and cerebrovascular disease.

24. Wang J, Zhang Y, Zhu Q, Liu Y, Cheng H, Zhang Y, Li T. Emodin protects mice against radiation-induced mortality and intestinal injury via inhibition of apoptosis and modulation of p53. Environ Toxicol Pharmacol 2016;46:311-8.

Abstract:

The aim of this study was to explore the protective effect of emodin, a plant-derived anthraquinone, against gamma radiation-induced mortality and intestinal injury in mice, and to investigate the radioprotective molecular mechanism. C57BL/6 male mice were pre-treated with emodin for 7days via oral gavage before gamma radiation. We found that pretreatment with emodin prolonged mice survival time after 9Gy total body irradiation (TBI). Mice were sacrificed at 1 week after 7Gy TBI, we found that emodin attenuated intestinal morphological changes and increased villus height, crypt numbers, and reduced villus and crypt apoptosis as well as inhibited the expression of p53. MTT assay, flow cytometry, Hoechst 33258 staining, real-time PCR, and Western blotting indicated that emodin pretreatment can effectively increase human umbilical venous endothelial cells (HUVECs) viability and attenuate cell apoptosis; it also inhibited the expression of p53, Bax, and Caspase3 in HUVECs after irradiation. In summary, these results suggest the potential of emodin as an effective radioprotectant against radiation-induced intestinal injury.

25. Chen W, Dong G, He S, Xu T, Wang X, Liu N, Zhang W, Miao C, Sheng C. Identification of benzothiophene amides as potent inhibitors of human nicotinamide phosphoribosyltransferase. Bioorg Med Chem Lett 2016;26(3):765-8.

Abstract

Nicotinamide phosphoribosyltransferase (Nampt) is an attractive therapeutic target for cancer. A Nampt inhibitor with novel benzothiophene scaffold was discovered by high throughput screening. Herein the structure-activity relationship of the benzothiophene Nampt inhibitor was investigated. Several new inhibitors demonstrated potent activity in both biochemical and cell-based assays. In particular, compound 16b showed good Nampt inhibitory activity (IC50=0.17 μM) and in vitro antitumor activity (IC50=3.9 μM, HepG2 cancer cell line). Further investigation indicated that compound 16b could efficiently induce cancer cell apoptosis. Our findings provided a good starting point for the discovery of novel antitumor agents.

26. Wan JJ, Qin Z, Liu X. ORM elevation in response to cognitive impairment is an accompanying phenomenon. CNS Neurosci Ther 2016; 22(8):723-4.

27. Sun Y, Zhang ZX, Liu X. Orosomucoid (ORM) as a Potential Biomarker for the

Diagnosis of Chronic Fatigue Syndrome (CFS). CNS Neurosci Ther 2016; 22(3):251-2.

28. Klionsky DJ, … Miao CY, …, Zughaier SM. Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). Autophagy 2016;12 (1):1-222