生物物理学报 2011, 27(4) 312-318 DOI: 10.3724/SP.J.1260.2011.00312 ISSN: 1000-6737 CN: 11-1992/Q

综述

基质金属蛋白酶在动脉粥样硬化易损斑块中的分子影像学研究

丁洁, 滕皋军

东南大学医学院，南京210009

摘要:

大量研究表明，依赖Ca^{2+}、Zn^{2+}等金属离子的基质金属蛋白酶在动脉粥样硬化斑块处的表达与斑块的稳定性密切相关，易损斑块处基质金属蛋白酶表达水平增高。单光子发射体层成像、近红外荧光成像、磁共振成像等分子影像学的方法，能够动态无创地检测动物模型动脉斑块或人颈动脉斑块切除后标本中基质金属蛋白酶的表达水平，不仅可以提示疾病的发展进程，而且能够评价药物的治疗效果。尽管大多数斑块成像的分子影像学手段尚未达到临床应用的阶段，但合成多模态的分子探针，综合运用各种不同的影像学方法将是动脉粥样硬化斑块成像的发展方向。

关键词: 分子影像 基质金属蛋白酶 斑块破裂

Molecular Imaging of Matrix Metalloproteinases in Vulnerable Plaque in Atherosclerosis

DING Jie, TENG Gaojun

School of Medicine, Southeast University, Nanjing 210009, China

Abstract:

Many researches indicate that the expression of matrix metalloproteinases(MMPs) in atherosclerotic plaques，whose activities involved with metal ions, such as Ca^{2+} or Zn^{2+}, is closely related to the stability of the plaques. There is an increased expression level of MMPs in vulnerable plaque. Molecular imaging methods, such as single photon emission computed tomography, near-infrared fluorescence imaging and magnetic resonance imaging provide dynamic and noninvasive ways in detectting the expression level of MMPs in the atherosclerosis plaque in the animal models or the tissue after carotid ectomy in patients. These methods can be used not only in prompting the progression of atherosclerosis but also evaluating the therapeutic effect of drugs. Although the majority of plaque imaging methods has not yet reached the stage of clinical application, the synthesis of multi-modality molecular probes and comprehensive use of different imaging methods will be the trend of atherosclerotic plaque imaging.

Keywords: Molecular imaging Matrix metalloproteinase Plaque rupture

收稿日期 2010-11-01 **修回日期** 2011-03-06 **网络版发布日期**

DOI: 10.3724/SP.J.1260.2011.00312

基金项目:

通讯作者: 滕皋军，电话：(025)83272121，E-mail：gjteng@vip.sina.com

作者简介:

作者Email: gjteng@vip.sina.com

参考文献：

1. Gross J, Lapiere CM. Collagenolytic activity in amphibian tissues: A tissue culture assay. Proc Natl Acad Sci USA, 1962, 48: 1014~1022
2. Rath T, Roderfeld M, Graf J, Roeb E. Matrix metalloproteinases in inflammatory bowel disease —— From basic research to clinical significance. Z Gastroenterol, 2009, 47: 758~769
3. Newby AC. Metalloproteinases and vulnerable atherosclerotic plaques. Trends Cardiovasc Med, 2007, 17:253~258
4. Chow AK, Cena J, Schulz R. Acute actions and novel targets of matrix metalloproteinases in the heart and vasculature. Br J Pharmacol, 2007, 152: 189~205

5. Kuge Y, Takai N, Ishino S, Temma T, Shiomi M, Saji H. Distribution profiles of membrane type-1 matrix metallo- proteinase (MT1-MMP), matrix metalloproteinase-2 (MMP-2) and cyclooxygenase-2 (COX-2) in rabbit atherosclerosis: Comparison with plaque instability analysis. Biol Pharm Bull, 2007, 30: 1634~1640
6. Brown DL, Hibbs MS, Kearney M, Loushin C, Isner JM. Identification of 92-kD gelatinase in human coronary atherosclerotic lesions. Association of active enzyme synthesis with unstable angina. Circulation, 1995, 91:2125~2131
7. Galis ZS. Vulnerable plaque: The devil is in the details. Circulation, 2004, 110: 244~246
8. Khatri JJ, Johnson C, Magid R, Lessner SM, Laude KM, Dikalov SI, Harrison DG, Sung HJ, Rong Y, Galis ZS. Vascular oxidant stress enhances progression and angiogenesis of experimental atheroma. Circulation, 2004, 109: 520~525
9. Schafers M, Riemann B, Kopka K, Breyholz HJ, Wagner S, Schafers KP, Law MP, Schober O, Levkau B. Scintigraphic imaging of matrix metalloproteinase activity in the arterial wall in vivo. Circulation, 2004, 109: 2554~2559
10. Kopka K, Breyholz HJ, Wagner S, Law MP, Riemann B, Schroer S, Trub M, Guilbert B, Levkau B, Schober O, Schafers M. Synthesis and preliminary biological evaluation of new radioiodinated MMP inhibitors for imaging MMP activity in vivo. Nucl Med Biol, 2004, 31: 257~267
11. Kuge Y, Takai N, Ogawa Y, Temma T, Zhao Y, Nishigori K, Ishino S, Kamihashi J, Kiyono Y, Shiomi M, Saji H. Imaging with radiolabelled anti-membrane type 1 matrix metalloproteinase (MT1-MMP) antibody: Potentials for characterizing atherosclerotic plaques. Eur J Nucl Med Mol Imaging, 2010, 37: 2093~2104
12. Fujimoto S, Hartung D, Ohshima S, Edwards DS, Zhou J, Yalamanchili P, Azure M, Fujimoto A, Isobe S, Matsumoto Y, Boersma H, Wong N, Yamazaki J, Narula N, Petrov A, Narula J. Molecular imaging of matrix metalloproteinase in atherosclerotic lesions: Resolution with dietary modification and statin therapy. J Am Coll Cardiol, 2008, 52: 1847~1857
13. Ohshima S, Petrov A, Fujimoto S, Zhou J, Azure M, Edwards DS, Murohara T, Narula N, Tsimikas S, Narula J. Molecular imaging of matrix metalloproteinase expression in atherosclerotic plaques of mice deficient in apolipoprotein e or low-density-lipoprotein receptor. J Nucl Med, 2009, 50:612~617
14. Deguchi JO, Aikawa M, Tung CH, Aikawa E, Kim DE, Ntziachristos V, Weissleder R, Libby P. Inflammation in atherosclerosis: Visualizing matrix metalloproteinase action in macrophages in vivo. Circulation, 2006, 114: 55~62
15. Wallis de Vries BM, Hillebrands JL, van Dam GM, Tio RA, de Jong JS, Slart RH, Zeebregts CJ. Images in cardiovascular medicine. Multispectral near-infrared fluore- scence molecular imaging of matrix metalloproteinases in a human carotid plaque using a matrix-degrading metalloproteinase-sensitive activatable fluorescent probe. Circulation, 2009, 119: e534~536
16. Wasserman BA, Sharrett AR, Lai S, Gomes AS, Cushman M, Folsom AR, Bild DE, Kronmal RA, Sinha S, Bluemke DA. Risk factor associations with the presence of a lipid core in carotid plaque of asymptomatic individuals using high-resolution mri: The multi-ethnic study of atherosclerosis (MESA). Stroke, 2008, 39: 329~335
17. Saam T, Cai J, Ma L, Cai YQ, Ferguson MS, Polissar NL, Hatsukami TS, Yuan C. Comparison of symptomatic and asymptomatic atherosclerotic carotid plaque features with in vivo MR imaging. Radiology, 2006, 240: 464~472
18. Frank JA, Miller BR, Arbab AS, Zywicke HA, Jordan EK, Lewis BK, Bryant LH Jr, Bulte JW. Clinically applicable labeling of mammalian and stem cells by combining superparamagnetic iron oxides and transfection agents. Radiology, 2003, 228: 480~487
19. Amirbekian V, Aguinaldo JG, Amirbekian S, Hyafil F, Vucic E, Sirol M, Weinreb DB, Le Greneur S, Lancelot E, Corot C, Fisher EA, Galis ZS, Fayad ZA. Atherosclerosis and matrix metalloproteinases: Experimental molecular MR imaging in vivo. Radiology, 2009, 251: 429~438
20. Lancelot E, Amirbekian V, Brigger I, Raynaud JS, Ballet S, David C, Rousseaux O, Le Greneur S, Port M, Lijnen HR, Bruneval P, Michel JB, Ouimet T, Roques B, Amirbekian S, Hyafil F, Vucic E, Aguinaldo JG, Corot C, Fayad ZA. Evaluation of matrix metalloproteinases in atherosclerosis using a novel noninvasive imaging approach. Arterioscler Thromb Vasc Biol, 2008, 28: 425~432
21. Weissleder R, Stark DD. Magnetic resonance imaging of liver tumors. Semin Ultrasound CT MR, 1989, 10: 63~77

本刊中的类似文章

1．乔瑞瑞, 贾巧娟, 曾剑峰, 高明远.磁性氧化铁纳米颗粒及其磁共振成像应用[J]. 生物物理学报, 2011,27(4): 272-288
2．黄佳国, 曾文彬, 周明, 高峰.双模态分子影像探针研究进展[J]. 生物物理学报, 2011,27(4): 301-311
3．王亚斌, 王慎旭, 曹丰.动脉粥样硬化易损斑块的分子影像研究进展[J]. 生物物理学报, 2011,27(4): 319-326
4．吴晨希, 朱朝晖, 李方, 陈永辉, 景红丽.分子影像：转化医学的重要工具和主要路径[J]. 生物物理学报, 2011,27(4): 327-334
5．范伟伟, 王亚斌, 张荣庆, 李聪叶, 李霜, 曹丰.分子影像监测血管内皮细胞生长因子预处理促进体外和体内脂肪间充质干细胞存活与增殖的研究[J]. 生物物理学报, 2011,27(4): 345-354

文章评论

反馈人		邮箱地址	
反馈标题		验证码	0375