（上接第 3601 页）

扰素的环境中有关。这表明 IMPDH 特异性抑制剂单独或联合内源性干扰素可以促进 RR 自身抗体形成。

有研究发现，利巴韦林可以诱导组织培养细胞形成 RR[12]。Keppeke 等[20]并未在单独使用 Peg-IFN-α 或利巴韦林的患者体内发现 RR 抗体，但是 Peg-IFN-α 联合利巴韦林治疗 HCV 患者的 RR 抗体阳性率为 38%，并且无应答或复发的患者比获得持续病毒学应答的患者具有较高的 RR 抗体。更重要的是，在联合治疗停药后，患者体内的 RR 抗体还可以保留 6～12 个月[21]。除此之外，抗 RR 自身抗体阳性率可能与种族无关。有研究发现，美国 HCV 感染人群中，无应答和复发者的 RR 抗体滴度高于应答者，而意大利复发者 RR 抗体滴度高于无应答和应答者[11]。

综上所述，RR 抗体在 Peg-IFN-α 和利巴韦林联合治疗后无应答或者复发的 HCV 感染者体内较为常见。但是，目前尚有许多问题函待解决，如 RR 的空间结构及 RR 除了 CTPS1 和 IMPDH2 组成外，是否还有其他蛋白成分；利巴韦林在体外可以诱导 RR 的形成却不能在体内发挥同样的效应；检查 RR 蛋白试剂的灵敏度有待进一步提高等。除此之外，更应关注 RR 蛋白的功能，尤其是棒状和环状蛋白的功能，希望其能成为 HCV 感染治疗过程的动态监测指标，并指导临床用药。

参考文献

[1] Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection[J]. Nat Rev Gastroenterol Hepatol, 2013, 10(9): 553-562.

[2] Halliday J, Klenerman P, Barnes E. Vaccination for hepatitis C virus: closing in on an evasive target[J]. Expert Rev Vaccines, 2011, 10(5): 659-672.

[3] Zhu YZ, Qian XJ, Zhao P, et al. How hepatitis C virus invades hepatocytes: the mystery of viral entry[J]. World J Gastroenterol, 2014, 20(13): 3457-3467.

[4] Najera I. Resistance to HCV nucleoside analogue inhibitors of hepatitis C virus RNA-dependent RNA polymerase [J]. Curr Opin Virol, 2013, 3(5): 508-513.

[5] Simmonds P. Genetic diversity and evolution of hepatitis C virus-15 years on[J]. J Gen Virol, 2004, 85(Pt 11): 3173-3188.

[6] Heim MH, Thimme R. Innate and adaptive immune responses in HCV infections[J]. J Hepatol, 2014, 61(Suppl 1): S14-25.

[7] Kim SR, El-Shamy A, Imoto S, et al. Prediction of response to pegylated interferon/ribavirin combination therapy for chronic hepatitis C genotype 1b and high viral load[J]. J Gastroenterol, 2012, 47(10): 1143-1151.

[8] Carcamo WC, Satoh M, Kasahara H, et al. Induction of cytoplasmic rods and rings structures by inhibition of the CTP and GTP synthetic pathway in mammalian cells[J]. PLoS One, 2011, 6(12): e29690.

[9] Carcamo WC, Calise SJ, von Mühlen CA, et al. Molecular cell biology and immunobiology of mammalian rod/ring structures[J]. Int Rev Cell Mol Biol, 2014, 308(1): 35-74.

[10] Stinton LM, Myers RP, Coffin CS, et al. Clinical associations and otential novel antigenic targets of autoantibodies directed against rods and rings in chronic hepatitis C infection[J]. BMC Gastroenterol, 2013, 19(13): 50-59.

[11] Carcamo WC, Ceribelli A, Calise SJ, et al. Differential reactivity to IMPDH2 by anti-rods/rings autoantibodies and unresponsiveness to pegylated interferon-alpha/ribavirin therapy in US and Italian HCV patients[J]. J Clin Immunol, 2013, 33(2): 420-426.

[12] Thomas EC, Gunter JH, Webster JA, et al. Different characteristics and nucleotide binding properties of inosine monophosphate dehydrogenase (IMPDH) isoforms [J]. PLoS One, 2012, 7(12): e51096.

[13] Probst C, Radzimski C, Blöcker IM, et al. Development of a recombinant cell-based indirect immunofluorescence assay (RC-IFA) for the determination of autoantibodies against "rings and rods"-associated inosine-5′-monophosphate dehydrogenase 2 in viral hepatitis C[J]. Clin Chim Acta, 2013, 418(16): 91-96.

[14] Acay A, Demir K, Asik G, et al. Assessment of the Frequency of Autoantibodies in Chronic Viral Hepatitis[J]. Pak J Med Sci, 2015, 31(1): 150-154.

[15] Ferri C, Sebastiani M, Giuggioli D, et al. Hepatitis C virus syndrome: A constellation of organ-and non-organ specific autoimmune disorders, B-cell non-Hodgkin′s lymphoma, and cancer[J]. World J Hepatol, 2015, 7(3): 327-343.

[16] Yang DH, Ho LJ, Lai JH. Useful biomarkers for assessment of hepatitis C virus infection-associated autoimmune disorders[J]. World J Gastroenterol, 2014, 20(11): 2962-2970.

[17] Seelig HP, Appelhans H, Bauer O, et al. Autoantibodies against inosine-5′-monophosphate dehydrogenase 2-characteristics and prevalence in patients with HCV-infection [J]. Clin Lab, 2011, 57(9/10): 753-765.

[18] Satoh M, Chan EK, Ho LA, et al. Prevalence and sociodemographic correlates of antinuclear antibodies in the United States [J]. Arthritis Rheum, 2012, 64(7): 2319-2327.

[19] Feng X, Huang J, Liu Y, et al. Identification of interferon-inducible genes as diagnostic biomarker for systemic lupus erythematosus[J]. Clin Rheumatol, 2015, 34(1): 71-79.

[20] Keppeke GD, Nunes E, Ferraz ML, et al. Longitudinal Study of a Human Drug-Induced Model of Autoantibody to Cytoplasmic Rods/Rings following HCV Therapy with Ribavirin and Interferon-alpha[J]. PLoS One, 2012, 7(9): e45392.

[21] Covini G, Carcamo WC, Bredi E, et al. Cytoplasmic rods and rings autoantibodies developed during pegylated interferon and ribavirin therapy in patients with chronic hepatitis C[J]. Antivir Ther, 2012, 17(5): 805-811.

（收稿日期：2015-04-25　　修回日期：2015-06-26）