



## Letter to Editor

JMR 2021; 7(6): 167-168  
November- December  
ISSN: 2395-7565  
© 2021, All rights reserved  
www.medicinarticle.com  
Received: 06-10-2020  
Accepted: 05-11-2020

## JAK-STAT, p53 and mTOR: Important signaling pathways and proteins in COVID-19

**Jamshid Ayatollahi<sup>1,2</sup>, Ghazaleh Harirzadeh<sup>3</sup>, Marzieh Lotfi<sup>4</sup>, Mahdie Hamidfar<sup>1</sup>, Seyed Hossein Shahcheraghi<sup>1</sup>, Mohammad Dehghaniri<sup>5</sup>, Azam Fazilati<sup>6</sup>**

<sup>1</sup> Infectious Diseases Research Center, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup> Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>3</sup> Department of Biology, Science and Art University, Yazd, Iran

<sup>4</sup> Abortion Research Center, Reproductive Sciences Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>5</sup> Afshar Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>6</sup> Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

### Abstract

COVID-19 is a disease with dangerous pandemic in the world. Attempts continue for efficient therapies. Signaling pathways are key targets in future treatments. This letter introduces three main factors including JAK-STAT, p53 and mTOR.

**Keywords:** COVID-19, JAK-STAT, mTOR, p53.

Dear editor

The current appearance of the coronavirus disease 2019 (COVID-19) dangerous pandemic produced by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has generated a health problem in everywhere of the world [1, 2]. Researchers want to recognize the main signaling pathways in this disease that cause lungs inflammation and mortality [3].

Current improvements in the pathophysiology of COVID-19 infection has shown that patients with severe disease can progress toward cytokine release syndrome (CRS) caused by an enhance in interleukin (IL) is specified IL-6, IL-2, IL-7, IL-10. Thus, cytokine storm therapy has been suggested as an essential treatment in the acute rescue from COVID-19. Many cytokines in COVID-19 use a specific Janus Kinase (JAK)-mediated key Intracellular signaling pathway. Inhibition of JAK main enzyme, thus, is a remarkable and interesting therapeutic plan for CRS, which is a usual reason of different clinical consequences of COVID-19 [4]. Also, COVID-19 prompts inflammation process by the JAK/STAT signaling pathway resulting in employment of macrophages, monocytes, endothelial cells, lymphocytes and killer cells developing headed for cytokine storm condition. This creates numerous inflammatory factors in the host that conclude the disease harshness. The JAK/STAT pathway also facilitates immune answers through differentiation of T, B cells. To decrease inflammation, JAK/STAT inhibitors like Baricitinib, Ruxolitinib and Tofacitinib have been used that facilitate its activities by cytokine signaling suppressors and also inhibitors of triggered STAT. Generally, the key mechanism of inhibition of JAK/STAT signaling at molecular planes is a key hypothetical plan in COVID-19 therapy [5]. Mammalian target of rapamycin (mTOR) - a serine-threonine kinase- contributes in cellular growth and metabolism and has been established to be triggered in COVID-19 replication and infection development. Throughout virus replication mTOR, downstream goal genes types are stimulated lead to effective protein production and biosynthesis of ribosome. In dendritic cells of plasmacytoid, mTOR protein is a key factor in the relationship of protein myeloid differentiation main answer gene 88 (MyD88), interferon regulatory factor (IRF-7) and Toll-like receptor 9 (TLR9) resulting in the transcriptional triggering of interferon genes (typ-1). Remarkably, the crucial tumor-repressor p53 will undergo destruction through ubiquitin ligase encoded by virus and zinc-finger domain of CHY - comprising 1 resulting in an enhanced viral existence in the cells of the host. Therefore, the inhibitors of mTOR and p53 stimulators or microRNAs that utilities as p53 and can affect mTOR 3'-UTR may effectually prevent virus replication in the human lung cells and respiratory area. Thus, mTOR controllers and p53 stimulators-based medications are the possible therapeutic applicants or aims that can be used for COVID-19 therapy [6, 7].

### \*Corresponding author:

**Dr. Seyed Hossein Shahcheraghi**

<sup>1</sup> Infectious Diseases Research Center, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup> Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Email:  
shahcheraghi@gmail.com

## REFERENCES

1. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *The Lancet infectious diseases* 2020; 20:533-534.
2. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; 579:270-273.
3. Li Y, Li H, Zhou L. EZH2-mediated H3K27me3 inhibits ACE2 expression. *Biochem Biophys Res Commun* 2020; 526:947-952.
4. Luo W, Li Y-X, Jiang L-J, Chen Q, Wang T, Ye D-W. Targeting JAK-STAT signaling to control cytokine release syndrome in COVID-19. *Trends Pharmacol Sci* 2020; 41:531-543.
5. Satarker S, Tom AA, Shaji RA, Alosious A, Luvis M, Nampoothiri M. JAK-STAT pathway inhibition and their implications in COVID-19 therapy. *Postgrad Med* 2021; 133:489-507.
6. Ramaiah MJ. mTOR inhibition and p53 activation, microRNAs: The possible therapy against pandemic COVID-19. *Gene reports* 2020;100765.
7. Appelberg S, Gupta S, Svensson Akusjärvi S, Ambikan AT, Mikaeloff F, Saccon E, et al. Dysregulation in Akt/mTOR/HIF-1 signaling identified by proteo-transcriptomics of SARS-CoV-2 infected cells. *Emerging microbes & infections* 2020; 9:1748-1760.