1. No.
   2019G002

2. Title
   S100A8/A9 cooperatively functions with neutrophil extracellulartraps in awakening of dormant cancer cells and their subsequent acquisition of metastatic ability in the lung which our novel biologics prevents

3. Period
   2019-2021

4. Summary
   Compiling evidence indicates that the neutrophils' NETs induced by LPS in the tobacco smoke will highly contribute to cancelling dormancy of the metastasized cancer cells, which leads cancer progression at the metastatic area with unexpectancy. In this subject, we focused on S100A8/A9 since it is highly released from the NETs-formed neutrophils in response to LPS stimulation and acts to promote cancer metastasis. We therefore aimed to study if S100A8/A9 from neutrophils will play an important role in cancer metastasis with cancelling dormancy. In this study, we revealed that S100A8/A9 is highly released from the LPS-stimulated neutrophils that form NETs which in turn functions to promote metastatic outgrowth *in vitro* as well as *in vivo*, probably contributing to awakening of cancer cells from dormancy state. The mechanistic analysis at molecular levels revealed the involved cascade to the S100A8/A9-mediated event, that is, S100A8/A9-MCAM-TPL2-ETV4 axis. In addition, our developed biologics (S100A8/A9 neutralizing antibody and exMCAM-Fc decoy) that both target S100A8/A9 act to impede the LPS-mediated cancer metastasis. These results may shed light on well figuring out the complex mechanism(s) of cancer metastasis with cancer dormancy and its therapeutic regulation.