Summary

Respiratory syncytial virus (RSV) is the most important cause of viral lower respiratory tract illness (LRI) in infants and children worldwide. Unfortunately, development of vaccines against this virus has been fraught with difficult obstacles. Moreover, there are only limited options for treatment of the disease, hence the need to search for novel therapeutic and vaccine prophylactic options against the RSV. In this study, interventionary measures against RSV infection and diseases have been evaluated. Firstly, antiviral actions of extract and compounds from Ramalina farinacea were evaluated as a way of identifying lead compounds with potencies against RSV. Secondly, a unique maternal vaccination approach as employing genetic vaccines encoding the RSV fusion F-protein were analyzed for possible interventions against RSV infection and disease. Mechanism of anti-RSV action of isolated compounds and extract was evaluated by time-of-addition studies and virus inhibitory and inactivation effects. To analyze trans-maternal immunity following maternal vaccination use was made of different genetic vaccines and analyzed the immunogenicity and efficacy of transferred humoral immunity from mother to offspring. To distinguish between placental and breast milk transfer naïve mice pups were bonded to vaccinated foster mothers immediately one week after birth. After RSV challenge bronchoalveolar lavages (BALs) and lung homogenates (LHs) were collected from both mothers and pups. Samples were analyzed for IgG1, IgG2a, IgA, viral neutralization, and viral load in BALs and LHs. Preliminary investigations of an extract and compounds from Ramalina farinacea (RF) showed anti-RSV activities with IC₅₀ = 5.639µg/ml and a cytotoxic effect against utilized cell lines at TC₅₀ = 103.14µg/ml. Sekikaic acid a compound of RF showed most potent inhibition towards RSV A2 strain (IC₅₀ 7.73 µg/mL). The time of addition assay revealed that sekikaic acid interferes with viral replication at a viral post-entry step, which is more active than the control ribavirin at 4 hours postinfection addition. The outcome of immunization using genetic constructs
encoding the fusion F-protein reveal high neutralization antibodies observed in sera taken from pups of immunized mothers in comparison to control pups from untreated or control treated mothers. Significant reduction of viral load of young offspring from immunized mothers was over 10-120 fold relative to the control offspring after viral challenge. Thus, sekikaic acid may provide lead candidate for the development of an optimized natural-based therapeutic agent against RSV infections.

Moreover, continued effort towards RSV vaccine development should be pursued especially the maternal vaccination as a proof-of-concept to protect the infant babies against this severe virus infection.