S49-2 Control of influenza virus based on functional structures

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The influenza virus genome (vRNA) consists of eight-segmented and negative-stranded RNAs. The vRNAs exist as viral ribonucleoprotein (vRNP) complexes associated with viral RNA-dependent RNA polymerases and nucleoprotein (NP). The vRNP complex is the basic unit for replication and transcription of the viral RNA genome in the cell nucleus. These virus genome-encoded factors should be good candidates for drug targets, so that we have been characterizing their molecular properties not only by biochemical and molecular biological methods but also at the basis of genetics and structure biology. In addition, host factors are required for the maximal RNA synthesis. We have been identifying and characterizing host factors involved in replication and transcription of the viral RNA genome by dissection and reconstitution of established *cell-free* systems and using a newly developed viral replicon system in yeast cells. With these systems, we identified RAF-1/Hsp90, IREF-1/MCM complex, and IREF-2 as factors for the viral RNA polymerase in its stabilization and chaperone for nuclear localization and assembly, stimulation of replication reaction, and activation of the second replication step, respectively. For NP, RAF-2p48/NPI-5/UAF/BAT1, RAF-2p36, and Tat-SF1 were identified as factors involved in formation of vRNA-NP complexes. The interaction between viral and host factors is to be the other drug target. Trials for anti-influenza virus drug discovery based on the structural aspect will be discussed.