I. INTRODUCTION

1.1 Background

Liver cancer, known as hepatocellular carcinoma (HCC), is ranked as the fifth most common cancer globally and claims the second spot in cancer-related deaths with over 900,000 new cases and more than 830,000 deaths in 2020 (Asafo-Agyei & Samant, 2023; Singal et al., 2023). The global incidence of liver cancer is expected to increase by 55% in 20 years, reaching a staggering 1.4 million cases and 1.3 million deaths in 2040, which is 56.4% higher than in 2020 (Singal et al., 2023).

Liver cancer tumorigenesis may occur due to multiple risk factors mainly triggered by chronic hepatitis B and C virus (HBV and HCV) infections as well as coinfection of hepatitis D (HDV), leading to genetic mutations and epigenetic changes (Lotfollahzadeh et al., 2023; Shen et al., 2023). Simultaneously, angiogenesis ensures a blood supply for tumor growth, while metabolic factors like obesity and diabetes influence the progression from conditions such as NAFLD to cancer (Pellegata et al., 2022; Sun & Karin, 2013). Furthermore, long-term alcohol consumption and cigarette smoking contributes to liver cancer by inducing cirrhosis, oxidative stress, inflammation, and direct DNA damage (Sun & Karin, 2013; Matsushita & Takaki, 2019). Lastly, exposure to aflatoxin B1, a potent carcinogen, initiates genetic mutations in liver cells, elevating susceptibility to liver cancer (Chu et al., 2018). These risk factors often synergize with viral infections like hepatitis B or C, further heightening the overall risk of hepatocellular carcinoma.

While there have been recent pharmacological advances in treatment, liver cancer remains one of the most challenging cancers to treat (Liu et al., 2015; Aref et al., 2016). The current management strategies for early-stage HCC include surgery, liver transplantation, and local thermal ablation therapies, whereas systemic medications like chemotherapy, sorafenib, lenvatinib, and further targeted therapies are used to treat advanced stages (Koulouris et al., 2021; Liu et al., 2023; Kudo,

2022). However, in order to improve the prognosis for HCC, the development of novel, targeted, non-toxic treatments are urgently needed (Liu et al., 2023).

Oncolytic viruses refer to viruses that have been genetically altered to replicate selectively within tumor cells, causing their destruction while sparing normal tissues (Aref et al., 2016; Chen et al., 2017). According to Chen et al. (2017), therapies using oncolytic viruses (OVs) can trigger an immune response against tumors. This is further supported by a recent study from Keller & Bell (2016) that demonstrated the critical role of antitumor immunity in the overall efficacy of oncolytic virotherapy. To enhance antitumor immunity, OVs are modified to express tumor-associated antigens, stimulating specific immune responses, or cytokines, amplifying immune cell activation (Chen et al., 2017). Numerous investigations, as reported by Aref et al. (2016), focus on eleven viruses, including adenovirus, vaccinia virus, coxsackievirus, reovirus, and measles virus (MV), which have entered clinical trials for treating various advanced cancers.

Specifically, measles virus (MV) is characterized as an enveloped virus containing a non-segmented, negative-strand RNA genome (Sugiyama et al., 2013). MV is equipped with two envelope glycoproteins, the hemagglutinin (H) and fusion (F) proteins, where the H protein directly interacts with cellular receptors, triggering the activation of the F protein to begin membrane fusion (Sugiyama et al., 2013). Several preclinical investigations have revealed the anti-HCC properties of engineered measles virus (MV). Blechacz et al. (2006) identified MV's capability to induce oncolytic effects in human HCC cell lines both *in vitro* and *in vivo*. Similarly, Lampe et al. (2013) alsoillustrated that MV-based suicide gene therapy presents a promising and innovative treatment approach for HCC, overcoming resistance to conventional therapy. Another study by Ong et al. (2013) further supports the viability of oncolytic MV as a strategy to significantly impede tumor growth in a majority of potential cancer patients. Nevertheless, additional research is essential to refine MV as an oncolytic vector and ascertain its potential as a therapeutic option for HCC.

1.2 Scope of Research

This project encompassed cell culturing of Huh-7 and B95a cell lines, viral production of measles virus (MV-FLuc), viral titration of MV-FLuc, cytotoxicity assay of MV-FLuc towards Huh-7 cell line, and the evaluation of apoptotic activity of MV-FLuc towards Huh-7 cell line using western blot analysis and flow cytometry.

1.3 Objectives and Hypothesis

The aim of this research is to investigate the role of measles virus (MV) as an oncolytic vector in liver cancer for future treatment strategies. It is hypothesized that measles virus (MV) will be able to effectively induce apoptosis in the Huh-7 cancer cell line and be utilized as an oncolytic vector against Huh-7 cell line.