

GS3-3 Application of bioactive mutant TNF- α to mucosal vaccine adjuvant

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Mucosal vaccination capable of stimulating mucosal immune responses would be the prophylactic strategy of choice against mucosally-transmitted infectious agents, such as human immunodeficiency virus (HIV) and influenza virus. However, despite the attraction of this approach, it has proven difficult to use in clinical practice. The development of a safe and effective mucosal adjuvant is a crucial step towards developing an effective mucosal vaccine. Much work has suggested that many candidates, such as cholera toxin and cytokines, show limited adjuvant activities and cause severe side effects. This is at least partly because these molecules have very low stability and need to be administered frequently. Therefore, to overcome this problem, the use of new technology to design effective practical adjuvants is necessary. To this end, we have isolated a bioactive lysine-deficient mutant tumor necrosis factor (mTNF-K90R) from phage libraries and have demonstrated that this possesses greater bioactivity than the wild-type molecule. This was associated with a higher protein stability because of the lower isoelectric point of the mTNF-K90R. These results suggested that mTNF-K90R could represent a novel mucosal adjuvant. Here, we have evaluated the efficacy and safety of mTNF-K90R as a mucosal adjuvant and have verified that our technique for creating bioactive mutant cytokines might be an attractive general approach for designing novel adjuvants.