A general understanding of the interactions between DNA and oppositely charged agents has given us a basis for developing novel DNA gel particles based on associative phase separation and interfacial diffusion [1]. In this context, two cationic proteins, lysozyme (LS) and protamine sulfate (PS) have been used as carriers to form DNA gel particles by interfacial diffusion [2]. It has been shown that DNA was effectively entrapped in the mixed protein solutions, protecting its secondary structure. A significant increase in the degree of effective entrapment of DNA has been achieved by mixing the two proteins. Controlling the magnitude of the DNA release and achieving controlled release systems were accomplished by changing the LS/PS ratio in the protein solution where particles were formed.

When used as DNA carriers, understanding the interactions with blood and cells forms the basis of fundamental in vitro studies. Determination of the haemolytic properties is one of the most common tests in studies of substances in solution and their interaction with blood components. Likewise, the in vitro cytotoxicity assays include the addition to the cells lines of the test compound at the required concentration range. However, the unique physicochemical properties of these DNA gel particles may cause their interactions with erythrocytes or cells to differ from those observed for conventional systems, and may also cause interference with standardized in vitro tests. The purpose of this work was to evaluate the in vitro DNA release, hemolytic activity, cytotoxicity and cellular uptake of these protein-DNA gel particles prepared at both millimeter and nanometer scale. Analysis of the data indicates that the binding characteristics of these two proteins, with different total charge and linear charge density are important parameters for the final properties of the obtained particles.