Abstract Submitted
for the MAR14 Meeting of
The American Physical Society

Phase Transitions in Antibody Solutions: from Pharmaceuticals to Human Disease YING WANG, ALEKSEY LOMAKIN, GEORGE BENEDEK, MIT, DANA FARBER CANCER INSTITUTE COLLABORATION, AMGEN INC. COLLABORATION — Antibodies are very important proteins. Natural antibodies play essential role in the immune system of human body. Pharmaceutical antibodies are used as drugs. Antibodies are also indispensable tools in biomedical research and diagnostics. Recently, a number of observations of phase transitions of pharmaceutical antibodies have been reported. These phase transitions are undesirable from the perspective of colloid stability of drug solutions in processing and storage, but can be used for protein purification, X-ray crystallography, and improving pharmokinetics of drugs. Phase transitions of antibodies can also take place in human body, particularly in multiple myeloma patients who overproduce monoclonal antibodies. These antibodies, in some cases, crystallize at body temperature and cause severe complications called cryoglobulinemia. I will present the results of our current studies on phase transitions of both pharmaceutical antibodies and cryoglobulinemia-associated antibodies. These studies have shown that different antibodies have different propensity to undergo phase transitions, but their phase behavior has universal features which are remarkably different from those of spherical proteins. I will discuss how studies of phase behavior can be useful in assessing colloid stability of pharmaceutical antibodies and in early diagnostics of cryoglobulinemia, as well as general implications of the fact that some antibodies can precipitate at physiological conditions.

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Date submitted: 15 Nov 2013 Electronic form version 1.4