Liquid-liquid Separation in Solutions of Normal and Sickle Cell Hemoglobin

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ABSTRACT

We show that in solutions of human hemoglobin—oxy- and deoxy- HbA or S—of near-physiological pH, ionic strength and Hb concentration, liquid-liquid (L-L) phase separation occurs reversibly and reproducibly at temperatures between 35 and 40 oC. In solutions of deoxy-HbS, we demonstrate that the dense liquid droplets facilitate the nucleation of HbS polymers, whose formation is the primary pathogenic event the sickle cell anemia. In view of recent results that shifts of the L-L separation phase boundary can be achieved by non-toxic additives at molar concentrations up to 30´ lower than the protein concentrations, these findings open new avenues for the inhibition of the HbS polymerization.