Background: Evidence from the United States and Europe supports the hygiene hypothesis—exposure to infectious agents during immune system development protects against immune-mediated disorders (allergy and autoimmunity). An evolutionary perspective suggests that this protection may represent adaptive priming in immune system development, evolved to tailor immune responses to the local infectious disease (ID) ecology and/or to minimize risk of immune-mediated disease. This project evaluated 1) the utility of biomarkers of immunocompetence (cell-mediated reactivity to pathogen antigen); 2) the association between early exposure to infectious agents and allergy; and, 3) the association between early exposure to infectious agents and immunocompetence among children in Kilimanjaro, Tanzania. Methods: Biomarkers of immunocompetence and allergy, diagnosed allergy, and indicators of early exposure to infectious agents (family size, housing materials, BCG vaccination, and hospitalization in infancy with infection) were evaluated among ~300 2-7 yo children. Results: Delayed-type hypersensitivity (DTH) to Candida albicans was associated with known predictors of immunocompetence (age and adiposity). Allergy was inversely associated with family size (OR: 0.24; 95% CI: 0.07, 0.85) and positively associated with earth housing materials (OR: 2.03; 95% CI: 1.21, 3.41) and hospitalization history (OR: 6.26; 95% CI: 1.84, 21.27). DTH was positively associated with family size (OR: 2.81; 95% CI: 1.04; 7.61), BCG vaccination (OR: 3.10; 95% CI: 1.10, 8.71), and hospitalization history (OR: 4.67; 95% CI: 1.00, 21.74). Conclusions: Allergy was inversely associated with family size, and positively associated with hospitalization and earth house materials, suggesting that during immune system development, routine ID (acquired from siblings) protect against allergy, while severe ID (requiring hospitalization) and soil-derived helminth infections (earth housing materials) promote allergy. These findings reflect Kilimanjaro’s complex ID ecology, and expand, rather than contradict, the hygiene hypothesis. Immunocompetence was positively associated with multiple measures of early exposure to infectious agents, supporting the hypothesis that immune development responds to early stimulation from infectious agents to enhance later protective immune responses to pathogen antigen. Together, these findings are consistent with the hypothesis that T helper type 1 (Th1)/Th2 regulation adapts to exposure to infectious agents during immune system development, with lasting consequences for both pathological and protective immune reactivity.