Despite the convergence of rapid technological advances in genomics and the maturing field of ecoimmunology, our understanding of the genes that regulate immunity in wild populations is still nascent. Previous work to assess immune function has relied upon relatively crude measures of immunocompetence. However, with next-generation RNA-sequencing, it is now possible to create a profile of gene expression in response to an immune challenge. In this study, captive zebra finch (*Taeniopygia guttata;* adult males) were challenged with bacterial lipopolysaccharide (2 mg/Kg BW; dissolved in 0.9% saline) or vehicle (0.9% saline) to stimulate the immune system. Two hours after injection, birds were euthanized. Hypothalami, spleen, and red blood cells (RBCs) were collected, and total RNA was isolated, sequenced, and partially annotated in these tissue/cells. The data show 249 significantly upregulated transcripts in the hypothalamus, as well as 267 and 86 in the spleen and RBCs, respectively, relative to controls. Also, 91 transcripts in the hypothalamus, 421 in the spleen, and 26 in the RBCs were significantly down-regulated. More specifically, a number of immunity-related transcripts (e.g., IL1B, RSAD2, SOCS1) were upregulated among tissues/cells. Additionally, some transcripts involved in the reproductive process (ESR1, NR5A1, ZP4) were down-regulated, suggesting a potential trade-off in expression of genes that regulate immunity and reproduction. These results suggest a novel transcriptomic response of bird nucleated RBCs to immune challenge. This could allow development of molecular biomarkers to rapidly screen bird populations by simple blood sampling in the field.