HLA-C2 (Human Leukocyte Antigen-C2) is a specific subset of human leukocyte antigen (HLA) molecules, which are proteins found on the surface of nearly all nucleated cells in the body. HLA molecules play a crucial role in the immune system by presenting fragments of foreign or abnormal proteins (antigens) to immune cells, such as T cells and natural killer (NK) cells. These immune cells use HLA molecules as a way to distinguish between healthy cells and cells that may be infected with pathogens or transformed into cancer cells.

HLA-C is one of the three major HLA class I gene groups, along with HLA-A and HLA-B. Within the HLA-C group, there are two major subsets: HLA-C1 and HLA-C2. HLA-C2 is characterized by the presence of certain HLA-C alleles, specifically HLA-C02, HLA-C04, HLA-C05, and HLA-C06, which have a common structural feature that distinguishes them from HLA-C1 alleles.

The main significance of HLA-C2 is its interaction with immune cell receptors, particularly killer cell immunoglobulin-like receptors (KIRs) found on NK cells. KIRs, including KIR2DL1, as mentioned earlier, can recognize and bind to specific HLA-C2 alleles. This interaction has important implications for immune responses and immune surveillance:

NK Cell Regulation: The interaction between KIR2DL1 on NK cells and HLA-C2 on target cells plays a role in regulating NK cell activity. When KIR2DL1 binds to HLA-C2, it delivers an inhibitory signal to the NK cell, preventing it from attacking healthy cells displaying HLA-C2. This helps maintain immune tolerance and prevents NK cells from mistakenly attacking the body's own cells.

Immune Response Against Infected or Cancerous Cells: In the presence of cells that have reduced or altered HLA-C2 expression (commonly seen in virus-infected cells or cancer cells), the inhibitory signal from KIR2DL1 is weaker or absent. This reduction in inhibition allows NK cells to become activated and target the abnormal cells for destruction.

Variations in HLA-C alleles, including the presence or absence of HLA-C2 alleles, can influence an individual's immune response and susceptibility to various diseases. The interplay between HLA-C2 and KIRs is a complex and important aspect of the immune system, with implications for infectious diseases, transplantation medicine, and cancer immunotherapy research.