Approximately 15 million babies yearly are born preterm – before the 37th week of pregnancy. The number of premature births in Poland increases every year - in 2015 it was 27865, while in 2017 even 30637. Since infections have been reported as responsible for up to 40% of preterm births and 80% of deliveries <30 weeks of gestation have evidence of infection, preterm delivery is considered the main complication of pregnancy. Furthermore, the ratio of infections at preterm neonatal care units is the highest amongst all pediatric units. Depending on the source, two ways of neonatal infections can be distinguished: intrauterine (inborn) and hospital-acquired. The high susceptibility of newborns to infection results from immaturity of the immune system. In neonates (especially in those born preterm), the important role in antimicrobial protection may play endogenous lectins. These are proteins with ability to recognise sugar residues being components of surface structures of numerous microorganisms (bacteria, fungi, viruses and protozoans). Among lectins, there are collectins and ficolins with generally similar structure organisation as well as biological activity. These proteins can contribute to the inhibition of infection by facilitating the absorption of microorganisms and killing them by specialized cells or by the activation of the so-called complement system. It should be emphasized that these proteins belong to the factors of innate immunity, which means that even in the first moments of life they can contribute to the effective control of infection. Well-characterized human collectins include mannose-binding lectin (MBL) and surfactant proteins A (SP-A) and D (SP-D), whose functions have been extensively studied. Three new collectins have recently been described: CL-L1 (CL-10), CL-K1 (CL-11) and CL-P1 (CL-12), but their clinical significance is still not well characterized. The aim of the proposed project is to clarify whether CL-L1 and CL-K1 contribute to the anti-infective protection of newborns, especially those born prematurely. These serum proteins form complexes (CL-LK). They facilitate the absorption of microorganisms by specialized killing cells by binding to them through the so-called sugar recognition domain (CRD), while the lysing of microorganisms occurs as a result of the activation of serine proteases complexed with CL-L1 and CL-K1. The highest expression of CL-K1 was found in the liver, kidney, adrenal gland and gallbladder (and to a lower extent, in lung, ovary, testis, and retina) whereas expression of CL-L1 was found mainly in the liver and adrenal gland. Interestingly, the high expression of both collectins was detected in placenta. The aim of the proposed project is to investigate the significance of CL-L1 and CL-K1, capable of recognizing molecular patterns associated with pathogens and activating the complement system in the protection of newborns (especially premature and low birthweight) against infections. The concentration of both proteins in cord blood sera of premature infants (including infants with infections during perinatal period) and healthy children born in time will be examined, and then their relation to gestational age, birthweight and the susceptibility to infection will be analysed. Polymorphisms of the *COLEC10* and *COLEC11* genes (influencing already demonstrated to influence CL-L1 and CL-K1 levels/activity) will be analysed and the frequency of variant alleles compared between preterm and term babies as well as between healthy neonates (no infection till hospital discharge) and newborns with early- and late-onset infections. The expression of afore-mentioned genes in decidua and chorionic villous in term placentas will be compared. Moreover, the influence of experimental viral infection on their expression in placentas will be tested. The association of expression of both genes with gestational age and the binding of tested proteins to bacterial isolates from preterm neonates will be tested also.

The assessment of the biological significance of CL-K1 and CL-L1 in newborns (and in the placenta) is expected to add significantly to the knowledge concerning neonatal susceptibility to infections and to allow estimation of potential usefulness of those collectins as biomarkers. The comparison of placental *COLEC10* and *COLEC11* gene expression in decidua and chorionic villi, comparison of their basal expression in placentas obtained from preterm and term labor as well as the expression in placentas experimentally infected with CMV and VSIV, will contribute to the significant extension of the knowledge concerning the regulation of synthesis of investigated proteins.