ImmunoTools *special* Award 2014

Maria Carmen Collado, PhD

IATA-CSIC, Dept. Biotechnology, Unit of Probiotics,
Av. Agustin Escardino nº7, 46980 Paterna, Valencia, SPAIN

Role of milk bioactive compounds on modulating NF-kB pathway

Our research group is interested in the search for new mechanisms involved in inflammation pathways. Necrotizing enterocolitis (NEC) is the leading cause of death from gastrointestinal disease in premature infants, and is characterized by a marked increase in acute inflammation of the intestinal mucosa that leads to epithelial cell death and systemic sepsis. NEC is the leading cause of death from gastrointestinal disease in premature infants, and is characterized by a marked increase in acute inflammation of the intestinal mucosa that leads to epithelial cell death and systemic. The pathogenesis of NEC is not known and there is no effective treatment for this disease, however, One hypothesis suggests that a major etiological factor for NEC is colonization of the neonatal gut with an abnormal microbiota. Recent studies suggest an association between the pattern of intestinal microbial species and NEC. It is known that soluble factors from *Lactobacillus casei* and *L. rhamnosus* prevent the intestinal epithelium from stress, such as inflammatory cytokines or super oxides, through stimulation of different signalling pathways. It has been described recently by our group that *L. casei* BL23 downregulated inflammatory genes in an ex-vivo human mucosa and triggered a global change of the transcriptional profile that indicated a clear homeostasis restoring effect and a decrease in signals produced by activated T cells. Furthermore, in an experimental NEC model, oral administration of a physiological dose of Epithelial Growth Factor (EGF) significantly reduces the incidence and severity of NEC. Further studies are necessary before EGF can be introduced as an efficient therapeutic approach of intestinal injury. In the GI tract, EGF enhances proliferation and differentiation of epithelial cells, but also has significant effects on healing of damaged mucosa or on intestinal adaptation after injury. Fetal intestine is exposed to EGF in amniotic fluid and in the postnatal period, the major sources of intestinal EGF are maternal colostrum and milk. Breast milk also contains other bioactive components such beneficial microorganisms, oligosaccharide and other compounds as IgA, other growth factors (EGF, TGF; GHFR; HB-EGF), cytokines and chemokines (e.g. IL-10, IL-6, IL-8, IL-1α, IL-3, IL-16, Gro-α, SDF-1α). However, the precise *in vivo* effects in the newborns and mechanisms of some of these bioactive agents remain to be determined.

We would like to use the recombinant growth factors, cyto-and chemokines from ImmunoTools for immunostimulation experiments in both, cultured intestinal epithelial

cells (IEC), Peripheral blood mononuclear cells (PBMC) and dendritic cells (DC) to evaluate their effect regarding inflammation score.

We are particularly interested in those cytokines which were previously shown to be present in higher concentrations in colostrum than in mature breast milk and which suggest to be important for neonates development and protection against diseases in the first days of life albeit the pro-inflammatory character of some of these cytokines. In a second part we will test for the effects of these cytokines in combination with probiotics (as *Bifidobacterium* and *Lactobacillus* spp. which have been also shown to be present in milk) and also with *Lactobacillus*-derived proteins as p40 and p75, known to interact with TLR-signalling pathways and thereby modulating NF-kappa B activity.