Support of anti-bacterial and anti-viral innate immune functions in vitro and in vivo by Immunel™, a novel extract from bovine colostrum whey.

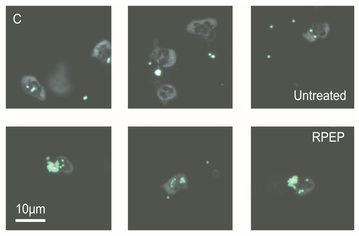
Steve G. Carter [1], Kathleen F. Benson[1], Dilip Patel [2], Gitte S. Jensen [2],
[1]NIS Labs, Klamath Falls, OR, [2]Sterling Technology Inc., Brookings, SD.

Background

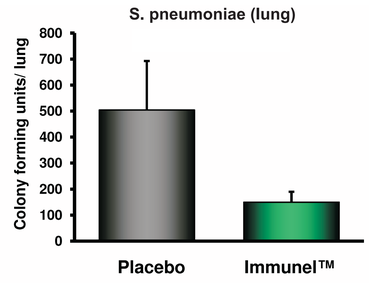
Colostrum is the biological fluid produced from the mammary glands of female mammals shortly after giving birth. The fluid has a distinct composition different from the milk produced afterwards. The composition of colostrum provides immediate immune protection to the newborn. The supportive properties of bovine colostrum when consumed by other mammalian species, including pigs and humans, are well documented in the literature. The immune modulating compounds in colostrum from farm animals have been receiving attention in a number of clinical applications. Immunel™ is an immunoglobulin-depleted lactose-reduced extract from colostral whey (bovine).

Immunel™ supports phagocytosis

Phagocytes are among our most immediate responders to bacterial invasion and immediately will initiate a series of events including migration towards the bacterial antigens or toxins, engulfing bacteria for destruction, and sending signals to alert the rest of the immune system to the invasion.



The direct effects of Immunel™ on separate aspects of our innate immune defense were tested in cell-based bioassays using human polymorphonuclear (PMN) cells. The pre-treatment with Immunel™ acted almost immediately, and within a few minutes after treating phagocytic cells with Immunel™, more cells were phagocytic, and each phagocytic cell consumed more particles.



Mice were infected with the human pathogen Streptococcus pneumonia, which causes infections in the upper respiratory tract, sinuses, and eyes. Animals treated orally with two doses of Immunel™ 30 minutes before and 4 hours after infection showed reduced bacterial load at 20 hours after infection, when compared to control animals. Thus, treatment with Immunel™ showed enhanced bacterial clearance as a result of antimicrobial activity in the animals.

Immunel™ supports distinct mechanisms of innate immune defense reactions

The 'Innate' part of our immune defense refers to the cellular defenses that act the quickest and most immediate. Many types of cellular reactions contribute to the immediate efforts to stop microbial invaders from taking hold in our body and causing disease.

These mechanisms include

- Phagocytosis, i.e. some of our cells are able to eat bacteria
- Recruiting immune cells into the area of infection
- Killing of our own cells if they have become transformed, such as being infected with a virus.

When Immunel™ was added to human immune cells in laboratory bioassays designed to approach these three functions, Immunel™ supported all three mechanisms.

Innate immune defense I:

Anti-bacterial properties.

Immunel affects phagocyte migration towards bacterial antigens as well as phagocytic activity.

Immunel Research Strategy

Identify mechanisms of action using cell-based bioassays

Verify actions in animal studies

Verify in a human clinical trial

Innate immune defense II:

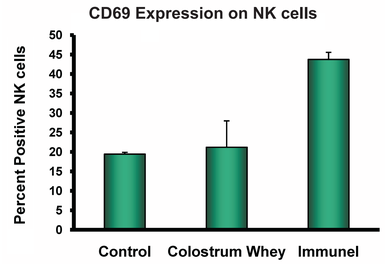
Anti-viral properties.

Immunel affects natural killer cell activation status, trafficking, and clearance of viral infection.

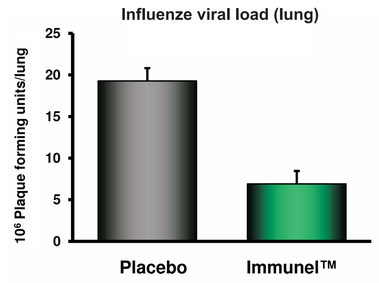
Immunel™ activates Natural Killer (NK) cells

Another type of immune cell that is able to respond immediately to invading pathogens is called an NK cell. These cells are able to attach to those of our cells that have become invaded by viruses, or transformed into cancer cells. The killing of the transformed cell can happen via cell-cell contact or by secretion of chemicals such as Perforin which helps destroy the malfunctioning target cell.

A human study found that nutritional supplementation with colostrum was equally efficient as a vaccine at preventing flu episodes.



Treatment of human NK cells with Immunel™ resulted in an activation of the NK cells. The treated NK cells expressed much higher amounts of an activation marker called CD69, which indicates that the NK cells were activated to be more efficient at attacking target cells.



Mice were infected with mouse-adapted influenza virus. Animals treated orally with a single dose of Immunel™ within 24 hours prior to infection showed reduced viral titer in the lungs, compared to control animals.

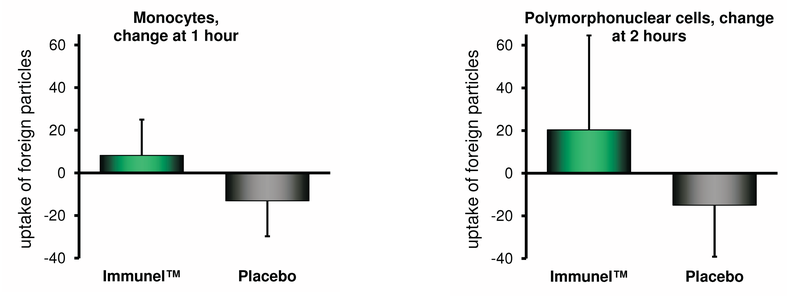
Human randomized double-blinded cross-over study

Human Clinical data

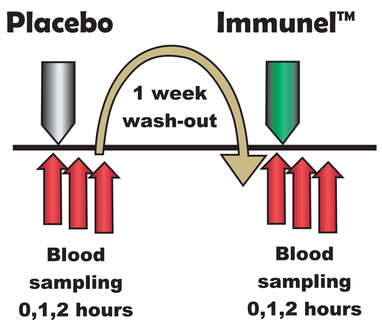
Study design: A randomized double-blinded placebo-controlled cross-over study design was used. Twelve healthy human subjects were tested on two different days at least one week apart. On each test day, subjects were fed either Immunel™ or placebo. At baseline and at 1 and 2 hours after consumption, blood samples were drawn.

Consumption of Immunel™ results in rapid increase in phagocytic activity in humans

Consumption of a single dose of Immunel™ resulted in a rapid increase in the phagocytic activity of human cells tested ex vivo at different time points after consumption. This was in contrast to the reduced phagocytic activity seen on the day when Placebo was consumed by the same people.



The difference in phagocytic activity between Immunel™ and Placebo was statically significant for monocytes at 1 hour after consumption ($P<0.25$) and for polymorphonuclear cells at 2 hours ($P<0.04$) after consuming a single dose of Immunel™.



Conclusion

Data identifying key mechanisms of action, combined with animal studies and human clinical data suggests that Immunel™ induces rapid changes in immune support, including specific mechanisms involved in anti-bacterial and anti-viral defenses.

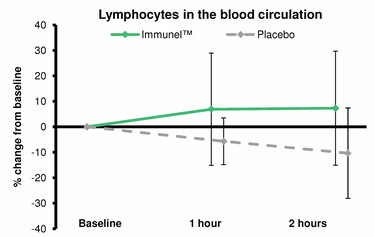
- Immunel™ supported distinct mechanisms of innate immune defense reactions.
- Immunel™ consumption reduced the severity of bacterial and viral airway infections in rodents.
- Immunel™ consumption induced potent and rapid changes in markers associated with the innate immune defense.

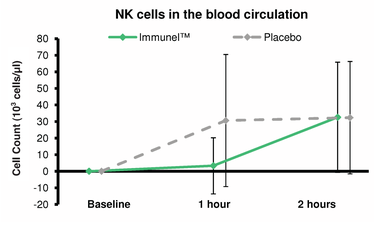
Consumption of Immunel™ provides a rapid, transient support for immune surveillance of human NK cells

NK cells are an important part of our anti-viral defenses, and these cells work primarily by surveying through tissue looking for target cells, which they then kill, either by contact or by secreting certain chemicals. The NK cells have very little activity in the blood circulation.

The study was conducted during the early/mid-morning hours on both study days. The increase in the numbers of circulating NK cells, seen with placebo, reflects part of natural circadian (day/night) fluctuations.

The delay in this increase (1 hour: $P<0.04$), seen after consumption of Immunel™, was selective for NK cells, since the total numbers of lymphocytes in the blood circulation increased after consumption of Immunel™ ($P<0.04$). This selective effect is suggestive of increased NK cell trafficking/homing, as a reflection of increased immune surveillance. This reflects that NK cells are retained in tissue more, scavenging for target cells.





Acknowledgements

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