

believe that the loss of p105 should if anything result in reduced inhibition of NF- κ B and consequently in diminished sensitivity to apoptosis induced by TNF α .

In my opinion, the increased sensitivity to TNF α -induced apoptosis that is observed in cells with silenced p105-expression is more likely to be due to a lack of p50-p65 heterodimers, which might not form in sufficient numbers if p50 levels are much reduced.

References

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Probiotics: time to move beyond Metchnikoff?

It is almost a century ago since Eli Metchnikoff proposed the, then revolutionary, idea to consume viable bacteria to promote health. Since that time, the area of what is now known as 'probiotics' has made dramatic progress, particularly during the past two decades. These two decades have also seen the emergence of a new, related, area of study – 'prebiotics'. The review by Touhy and co-workers in a recent issue of *Drug Discovery Today* [1] nicely summarizes the main achievements in these two fields and also indicates the future challenges.

The authors of the review restricted themselves to the effects of pre- and

probiotics in the gut. This is understandable because most of the work has been done on gastrointestinal tract-related disorders. However, the basic idea with pre- and probiotics is modulation of the activity and/or composition of the endogenous microbiota. Many other parts of the human body have an endogenous microbiota too. The potential health benefits that could be provided by probiotics in non-intestinal applications have to date received little attention [2].

The non-intestinal application of probiotics that has received most attention, albeit much less than intestinal probiotics, is that of use in urogenital tract-related disorders. The challenges for this kind of application of probiotics are to some extent similar to those for intestinal applications. Some studies have also used the oral administration of the preparation. Selected probiotics have been observed to be able to reduce the risk of urinary tract infections [3] indicating that this is a feasible approach.

A different application is to use oxalate metabolizing bacteria in the intestine to reduce the urinary load of oxalate, thereby diminishing the risk for the formation of calcium oxalate renal stones [4]. Although the application is still intestinal, the target is novel and outside of the intestine.

Modulation of the nasopharyngeal microbiota has also been found to be a potentially successful approach. Children who have experienced recurrent otitis media have been found to have reduced levels of α -haemolytic streptococci. Application of a nasal spray with six strains of α -haemolytic streptococci reduced the recurrence rate of otitis media [5].

Probiotics for the skin have been proposed but not yet investigated, either in experimental animals or in a clinical setting [6].

Metchnikoff founded the research field of probiotics, aimed at modulating

the intestinal microbiota. Have his ideas held us back to explore additional applications for probiotics? Although much work remains to be done on the intestinal applications of pre- and probiotics, the time has come to move on and extend Metchnikoff's ideas to other parts of the body with an endogenous microbiota. The above examples show that non-intestinal applications of probiotics can be successful and warrant further investigations.

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