

ProVen: Microbiota

PROVEN[®] PROBIOTICS

- Established in 1994 by biotechnologists Nigel and Sue Plummer – now more than 200 staff
- Internationally recognised as an innovator and premium quality manufacturer within the nutritional supplement industry
- Powerful combination of research scientists and award-winning research, together with formulation, process and production technologies
- Development and manufacture of nutritional food supplements for the healthcare market, supplying high specification products to the practitioner market of GPs and nutritionists
- Provides a fully integrative manufacturing service, involving unique formulations, innovative presentation and high quality finished products
- The company's products are sold in the UK, Norway, Israel, Canada and the USA



- VEGA and ProVen Probiotics are the brands owned by Cultech
- VEGA established more than 20 years ago
- ProVen Probiotics around 15 years old
- Access to a large team of scientists and researchers
- Constant innovation, research and development
- Recently published papers on Lab4 with vitamin C, vitamin D, glucosamine, plant sterols and omega 3, amongst others
- Strong links around the world – product development – new ProVen products, vitamin D



PROVEN[®]
PROBIOTICS

We have already made a difference to some premier brands worldwide

- Provides GNC with entire own label probiotic range
- Provides Boots with entire 'own label' probiotic range
- Supplies Holland and Barrett with their entire own brand
- Supplies Blackmores/Bioceuticals – the largest supplement brand in Australia
- Soon to supply NBTY.
- Provide 50% of the professional brands in North America and U.K

All Cultech 'Own Label' and the ProVen Brand
contain the

Lab4[®]
PROBIOTICS

Probiotic Consortium



To Understand Probiotics –
We Need To Have An Understanding of Our
Microbiota (Microbiome)

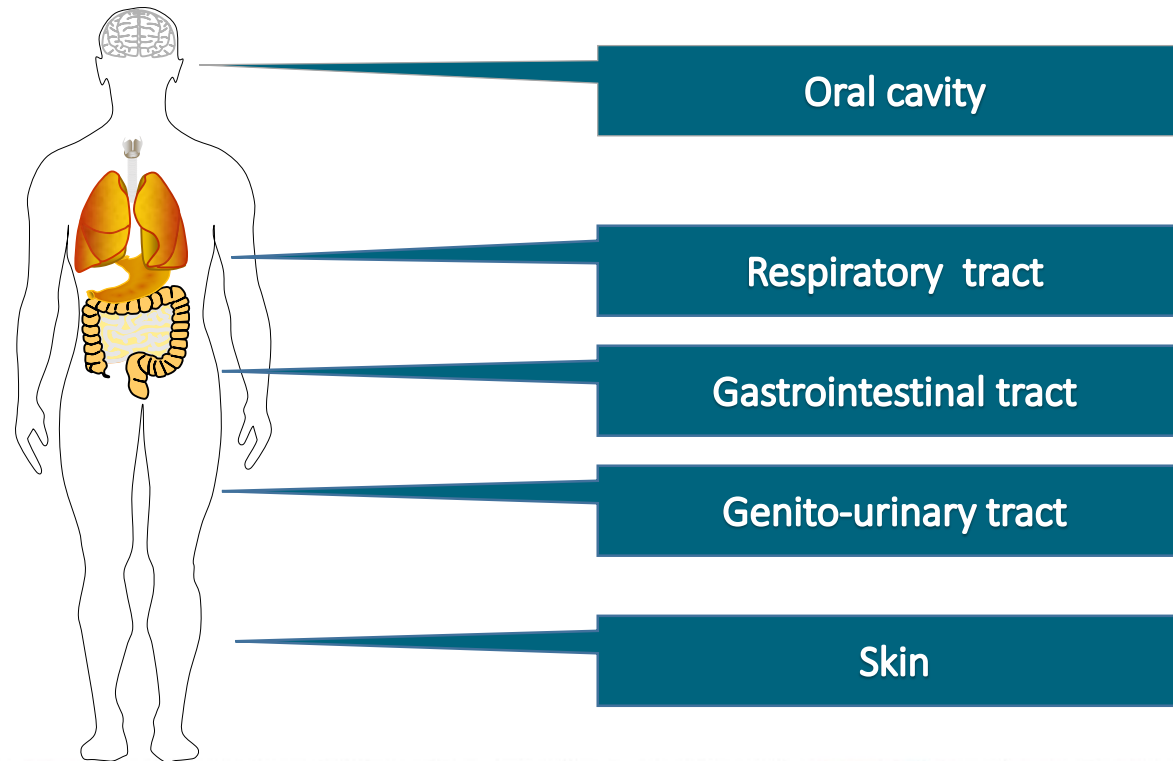
Our amazing microbiota – a constant companion and friend throughout our lives, without which, we would become ill and probably die within 5 years of birth!

So what is our microbiota?

Facts & Figures

- 100,000 billion viable microbes in the intestine with 2000 species and 7000 strains!
- 1,000 billion viable microbes on skin

Human Microbiota - Where Is It?



Interesting?

- Intestinal microbiota weighs about 1.5kgs
- Approximately 50% of faecal mass is bacterial biomass
- Microbiota produces about 2 litres of 'gas' per day
- Acquisition of resistance to antibiotics occurs in the intestine

The Normal Human Microbiota The First Colonisation Birth – 2 Days

The newborn infant is microbiologically sterile.

The newborn gut is a perfect microbial habitat – food, moisture, warmth

Its first flora is acquired from contamination/inoculation from the environment the neonate is born into:

- vaginal birth: vaginal, skin and rectal microflora of the mother
- C-section: skin and hospital environmental flora

Dominant Types:

Vaginal Birth

Lactobacilli: mainly 'acidophilus' types
Propionibacteria; Streptococci
Enterobacteria: various including E. coli

Minor colonisers

Bifidobacteria, Bacteroides, Clostridia

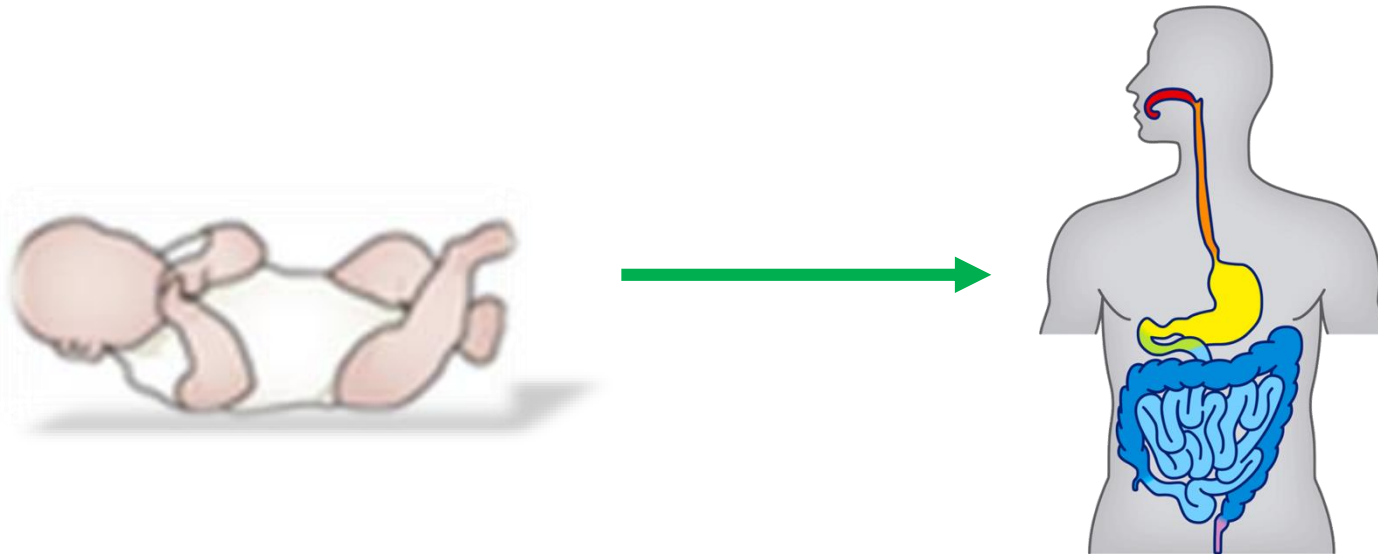
C-section

Staphylococci: S. aureus (MRSA)
Enterococci: E. faecium, E. faecalis
Enterobacteria

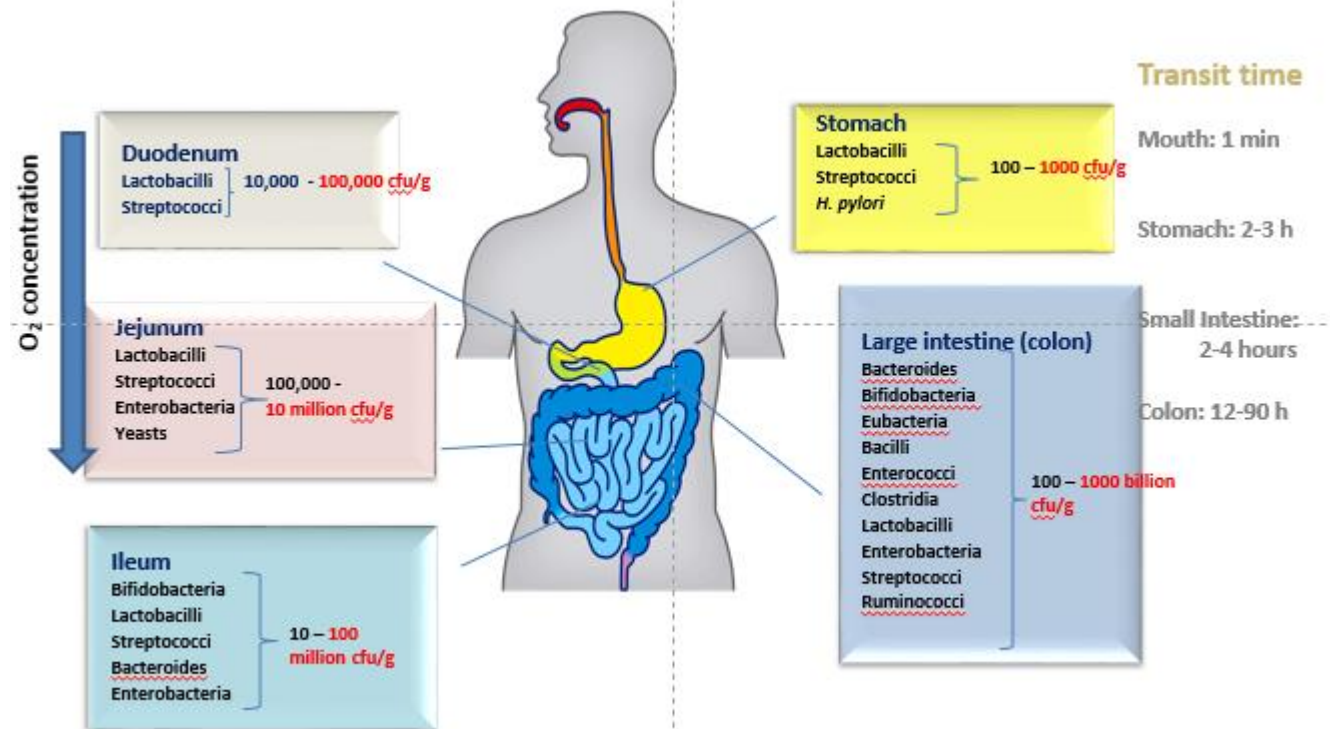
Lactobacilli

The Normal Human Microbiota – Infant to Adult

The intestinal microbiota acquires adult characteristics and is fully formed by two-three years of age. This process is driven by epigenetic factors and the intake of major food groups by this age.



Typical Microbiota of the Adult Gastrointestinal Tract



The Gut Microbiome – The Small/Large Intestinal Split

20 ft long - fast transit time (2-4 hours)

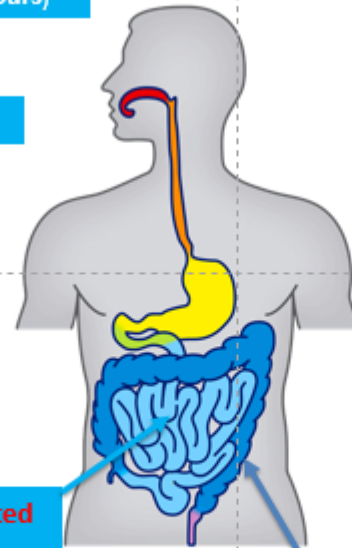
Site of major absorptive processes

Site of major immune, endocrine and enteric neural functionality

Site of major disruption of microbiome by antibiotics

Low microbial numbers dominated by facultative types (e.g. Lactobacilli, Coliforms)

Site of most activity of most probiotics (2-25 billion)



4 ft long – slow transit time (18-90 hours)

Minimal absorptive function

Site of some immune, endocrine, and neural functionality

Less disruption by most antibiotics

Huge microbial numbers dominated by obligate anaerobes (e.g. Bacteroides)

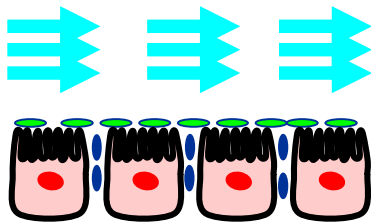
Very high potency probiotics required to yield effect (100 billion – 2000 billion)

Site of major activity of prebiotics

Why are there such major difference in small intestinal and large intestinal numbers of microbes?

Duodenum/Jejunum

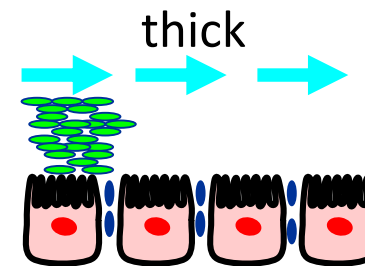
- Flow rate faster than replication rate
- Attachment compulsory for colonisation
 - Bacterial layer one cell thick



Fast Flow

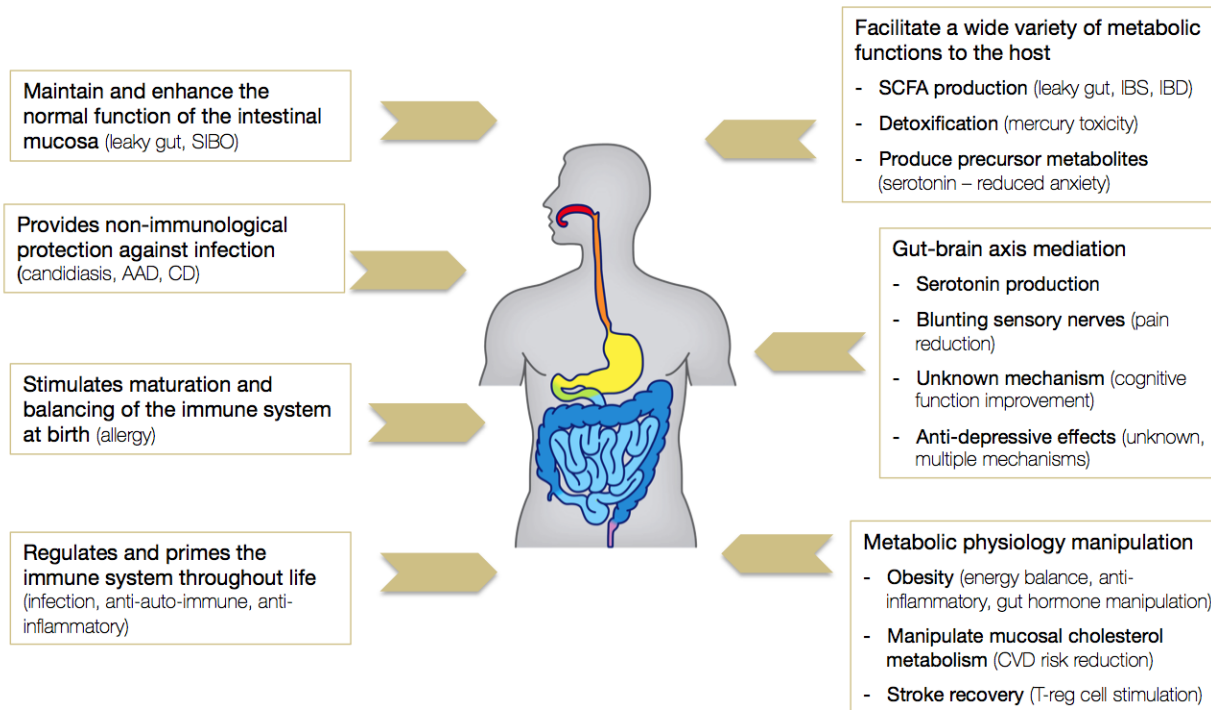
Colon

- Flow rate slower than replication rate
- Attachment non compulsory for colonisation
- Bacterial layer in mucous up to 200 cells thick



Slow Flow

What is the function of microbiota?



Manipulation/Disruption Of Human Microbiota

- ANTIBIOTICS
- PROBIOTICS
- PREBIOTICS
 - FMT