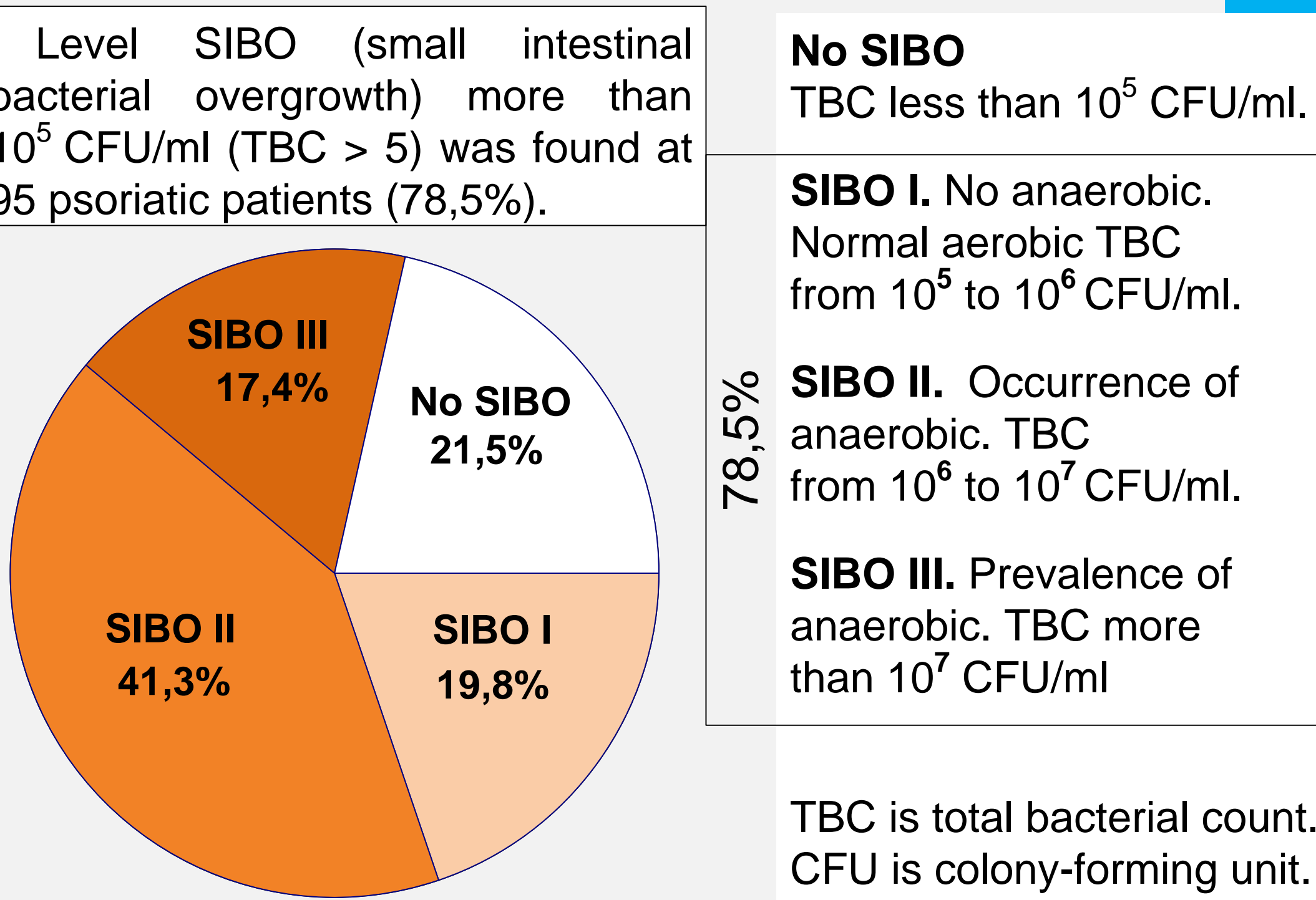


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For the first time researches of transient microflora of proximal small intestine at 121 psoriatic patients (PASI >=20) are conducted. There are 52 patients with moderate psoriasis (PASI in range 20-30) and 69 patients with severe psoriasis (PASI more than 30). At all patients psoriasis was in progressing stage. Control group consists of 43 healthy persons. For definition of species and subspecies of bacteria the method of bacteriological cultures on special mediums was used.

## SIBO severity level (121 psoriatic patients)



## Transient microflora of proximal small intestine

TBC for psoriatic patients has made - on average 3x10<sup>6</sup> CFU/ml (lg=6,49) that is much more than in the control group - on average 1,1x10<sup>3</sup> CFU/ml (lg=3,05). The correlation between SIBO level and PASI (r = 0,46), between SIBO level and duration of psoriasis disease (r = 0,43) has been found.

At 93% of psoriatic patients Bifidobacterium spp. was found - on average 2x10<sup>5</sup> CFU/ml (lg=5,3). In the control group at 40%, on average 250 CFU/ml (lg=2,41).

At 84% of psoriatic patients Lactobacillus spp. was found - on average 4,6x10<sup>4</sup> CFU/ml (lg=4,66). In the control group at 19%, on average 350 CFU/ml (lg=2,54).

At 79 of 121 psoriatic patients (65%) Enterococcus spp. was found - on average 2x10<sup>5</sup> CFU/ml (lg=5,28). Enterococcus spp. are not found in the control group at all. At part of psoriatic patients Str.pyogenes (9%) and Str.viridans (30%) were found (not found in the control group).

Microflora	Psoriatic patients (121 pers.)			Control healthy (43 pers.)		
	carrier	% of carrier	lg CFU/ml	carrier	% of carrier	lg CFU/ml
Bifidobacterium spp.	112	93%	5,3	17	40%	2,41
Lactobacillus spp.	102	84%	4,66	8	19%	2,54
Bacteroides spp.	20	17%	3,3	5	12%	2,86
E.coli typical	81	67%	5,04	11	26%	2,94
E.coli lactose-neg.	4	3%	3,62	0		
E.coli hemolytic	18	15%	3,6	0		
Enterococcus spp.	79	65%	5,28	0		
Str.viridans	36	30%	5,74	0		
S.aureus	18	15%	3,24	0		
Str.pyogenes	11	9%	4,81	0		
S.epidermidis	75	62%	5,54	17	40%	2,70
Candida	45	37%	4,76	10	23%	2,43
Acinetobacter spp.	7	6%	3,56	4	9%	2,40
Proteus spp.	24	20%	4,1	7	16%	2,14
Clostridium spp.	24	20%	5,2	0		
Klebsiella spp.	17	14%	3,13	0		
Moraxella spp.	63	52%	4,45	0		
<b>Total bacterial count</b>			<b>6,49</b>			<b>3,05</b>

## Other basic research projects

Many of psoriatic patients had malabsorption syndrome. Eugeny Kharkov with co-workers (from 2005 till now). Krasnoyarsk state medicine university, Krasnoyarsk, Russia.

Majority of psoriatic patients had high blood LPS-level. Zuhra Garaeva with co-workers (2005-7). Kazan Medicine Academy, Kazan, Russia.

Phagocytes tolerization (reprogramming) and their properties. Robert Sabat and Kerstin Wolk with co-workers (2000-2005) University Hospital Charité, Berlin, Germany.

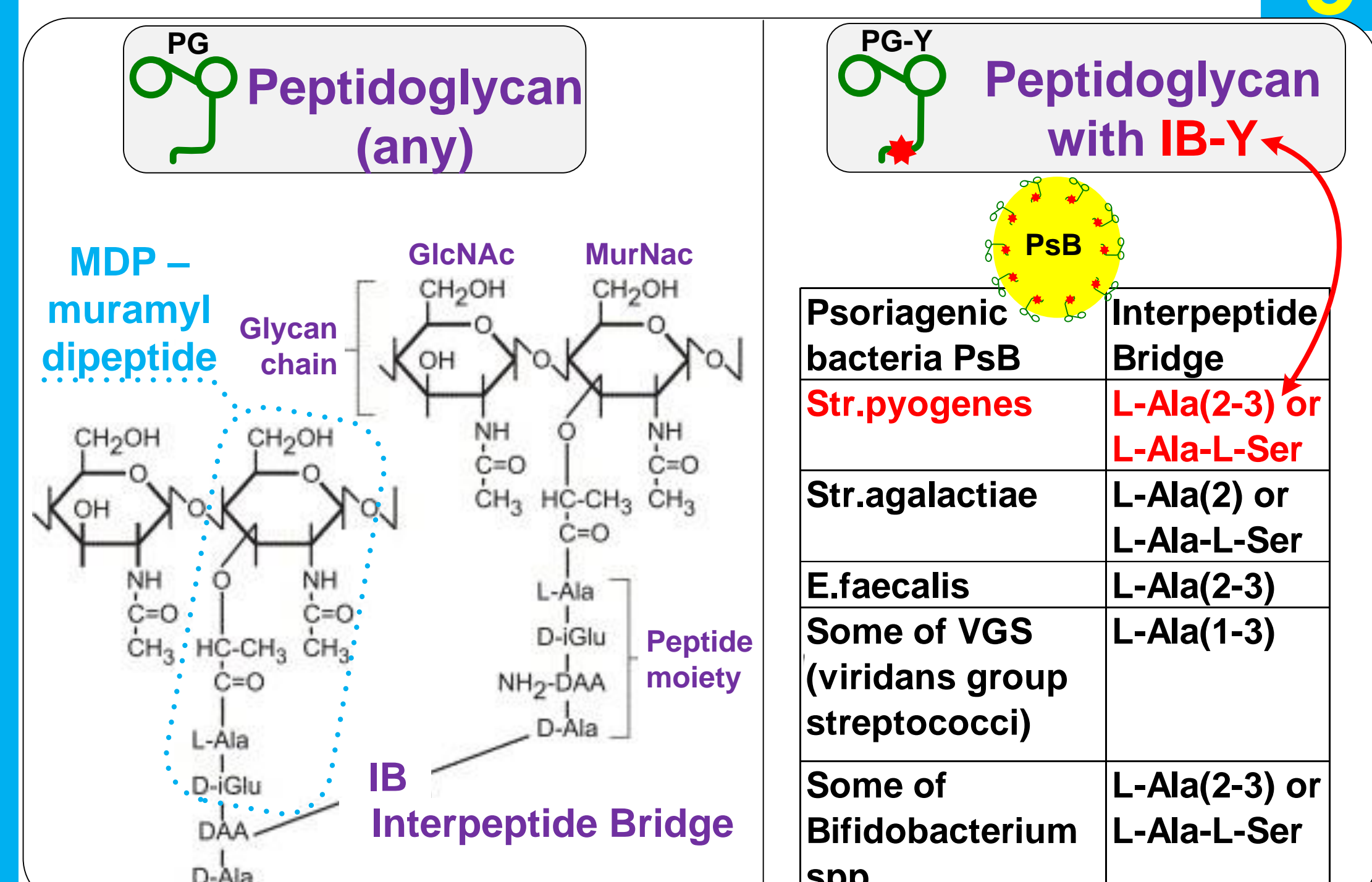
Jean-Marc Cavaillon with co-workers (from 2004 till now). Institut Pasteur, Paris, France.

## Systemic model of pathogenesis.

The antigenic role of streptococcal peptidoglycan outside skin (gut, tonsils, blood flow) and inside psoriatic skin. Barbara Baker and Lionel Fry (2006-7). Faculty of Medicine, Imperial College, London, UK.

Hypotheses are marked ?

## PG structure and PsB



Symbols	Y-antigen	LPS	Mo-T	DC-T	Mo-R	DC-R
★	Y-antigen = part(s) of interpeptide bridge IB-Y?	LPS = lipopolysaccharide, free and bound in complexes	Mo-T = tolerized monocytes. They are kPAMP-carriers.	DC-T = tolerized dendritic cells. They are kPAMP-carriers.	Mo-R = PG-Y(+)/Mo-T	DC-R = PG-Y(+)/DC-T
PG-Y	PG-Y = peptidoglycan A3alpha with interpeptide bridges IB-Y (but can contain and others also)	Gram(-) TLR4-active bacteria				
PsB	PsB = psoriogenic bacteria = Gram+ bacteria with peptidoglycan PG-Y.					
MF-R	MF-R = macrophages, derived from Mo-R					
MoDC-R	MoDC-R = dendritic cells, derived from Mo-R					
maDC-Y	maDC-Y = mature dendritic cells, presenting Y-antigen					

## Systemic psoriatic process SPP. Short description.

Increased colonization of small intestine by Str.pyogenes and others Gram+ bacteria with similar peptidoglycan (named psoriogenic bacteria PsB) and also by Gram(-) TLR4-active bacteria can play important role in psoriasis pathogenesis.

Fragments of bacterial products contain kPAMP (LPS and PG). kPAMP get to systemic blood flow, form chronically increased both kPAMP-level and kPAMP-load on blood phagocytes (i.e. PAMP-nemia).

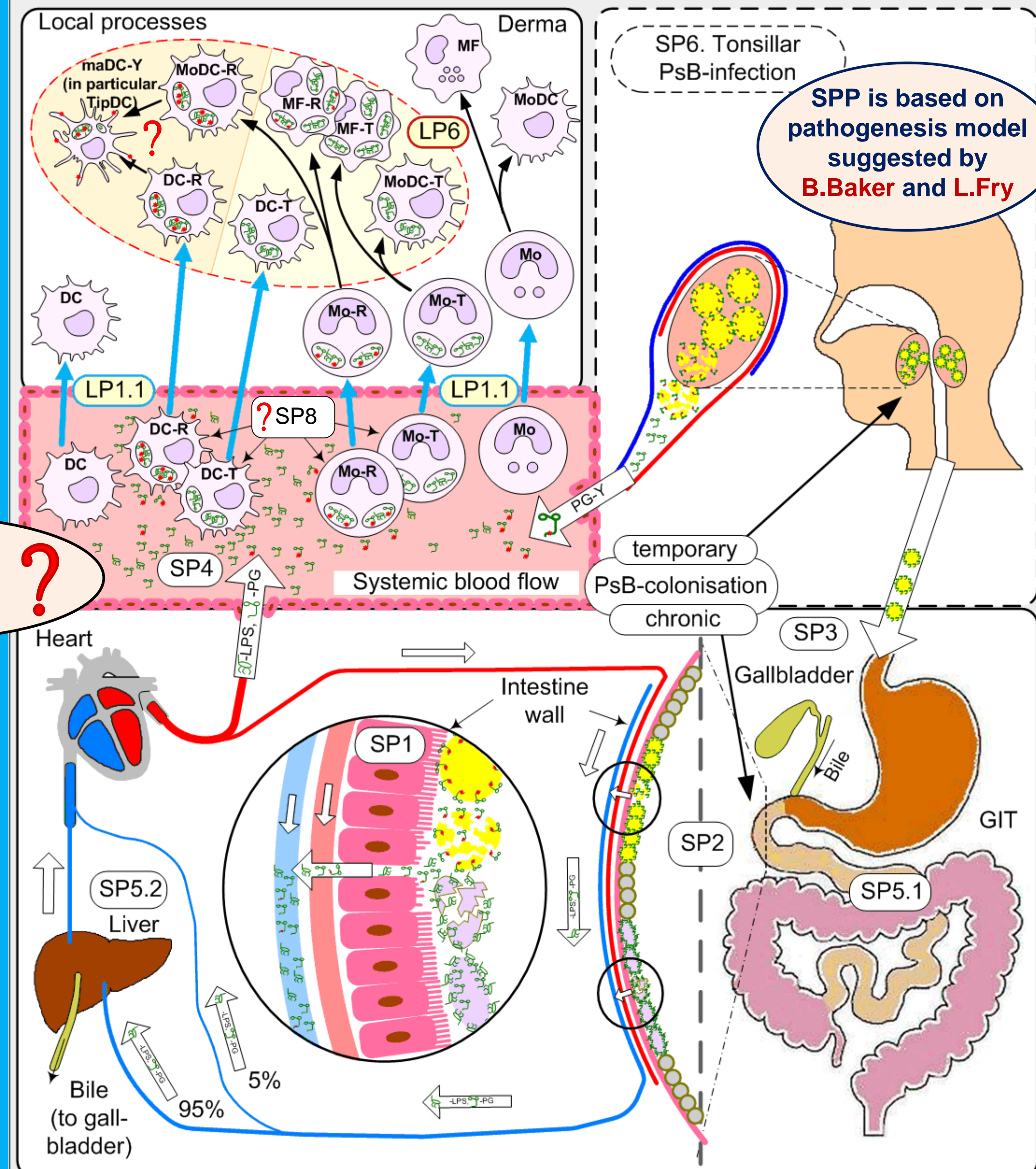
It provided growth of fractions of tolerized monocytes Mo-T and tolerized dendritic cells DC-T in blood flow. Tolerized Mo-T and DC-T as a rule are kPAMP-carriers. Some of them occurs (PG-Y)-carriers.

There are Mo-R = PG-Y(+)/Mo-T and DC-R = PG-Y(+)/DC-T.

Subprocess SP8.1 is growth of subfractions Mo-R and DC-R with increased (PG-Y)-carriage.

Systemic psoriatic process SPP operates if SP8.1 operates only. If tolerized Mo-R and DC-R getting into inflamed derma - they can be transformed into mature maDC-Y, presenting Y-antigen.

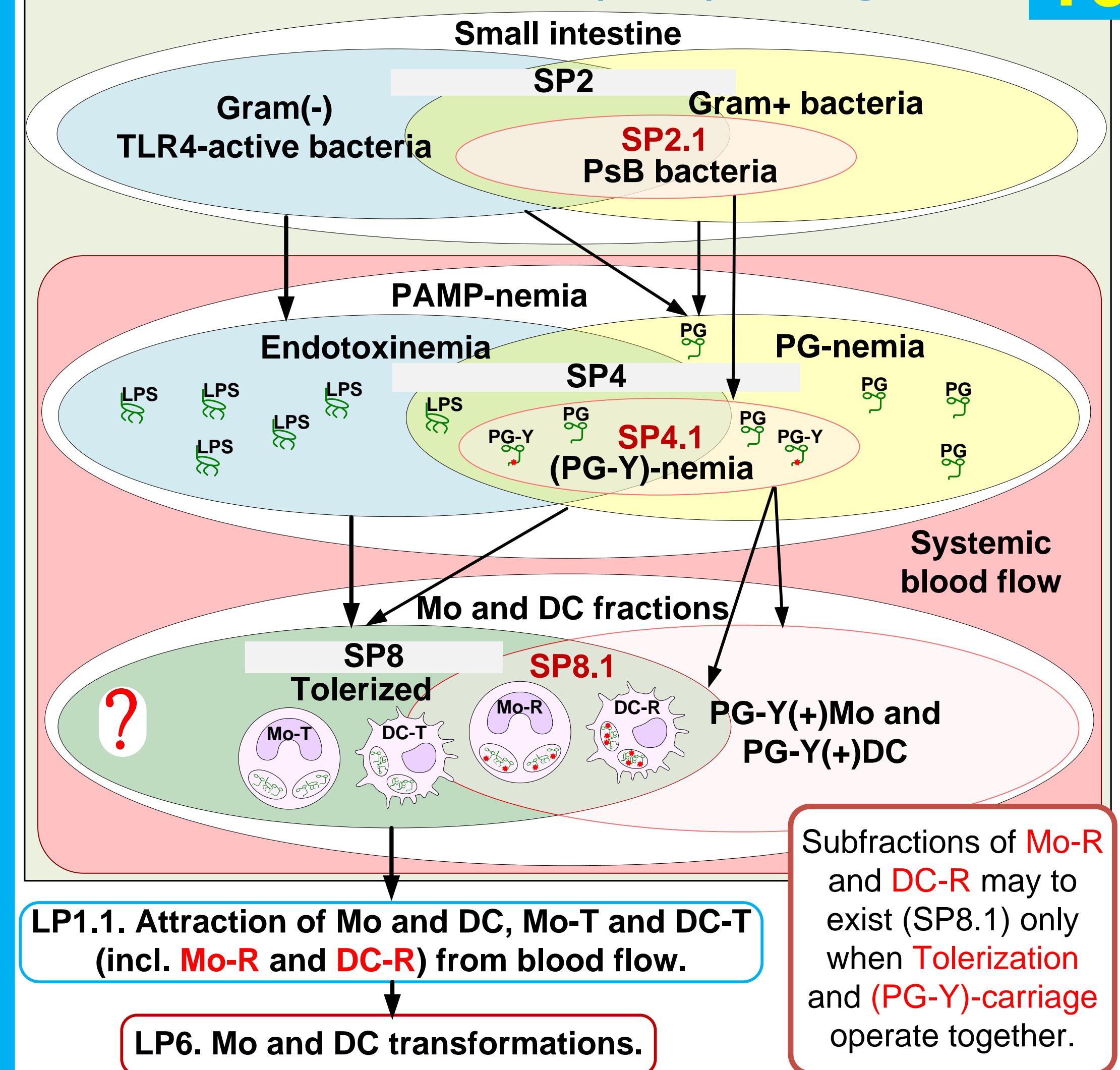
## Systemic psoriatic process SPP and some local processes. Illustration.



## SPP. Main systemic subprocesses.

**SP1.** Hyperpermeability of intestinal walls for bacterial products;  
**SP2.** Growth of populations of Gram+ (incl. psoriogenic PsB) and Gram(-) TLR4-active bacteria;  
**SP3.** Disturbance of production and/or circulation of bile acids;  
**SP4.** PAMP-nemia. Increased kPAMP-load on blood phagocytes. Increased kPAMP level in blood. The major kPAMP (key PAMP) - PG and LPS.;  
**SP4.1.** (PG-Y)-nemia;  
**SP5.** Overload and/or disorders of detoxication systems in intestine (**SP5.1**) and hepatobiliary system (**SP5.2**);  
**SP6.** Tonsillar PsB-infection;  
**SP8.** Growth of tolerized fractions Mo-T and DC-T. Increased kPAMP-carriage.;  
**SP8.1.** Growth of subfractions Mo-R and DC-R. Increased (PG-Y)-carriage.

## SPP-basis: Tolerization + (PG-Y)-carriage.



## Tolerized Mo-T and DC-T Are lowered

- Secretion of proinflammatory cytokines (TNF-alpha, IL-1beta, IL-12, etc.) after repeated PAMP-load.
- Expression of HLA-DR, CD74, HLA-DM, CD58 (LFA-3) and CD86 etc.
- Production and level of intracellular proteins cathepsin S and legumain, which are responsible for splitting and processing of antigens.
- Production, transport and expression of MHC II
- Ability to presentation of antigens and activation of T-lymphocytes.

Raised level of intracellular protein IRAK-M, the general manager of tolerization.

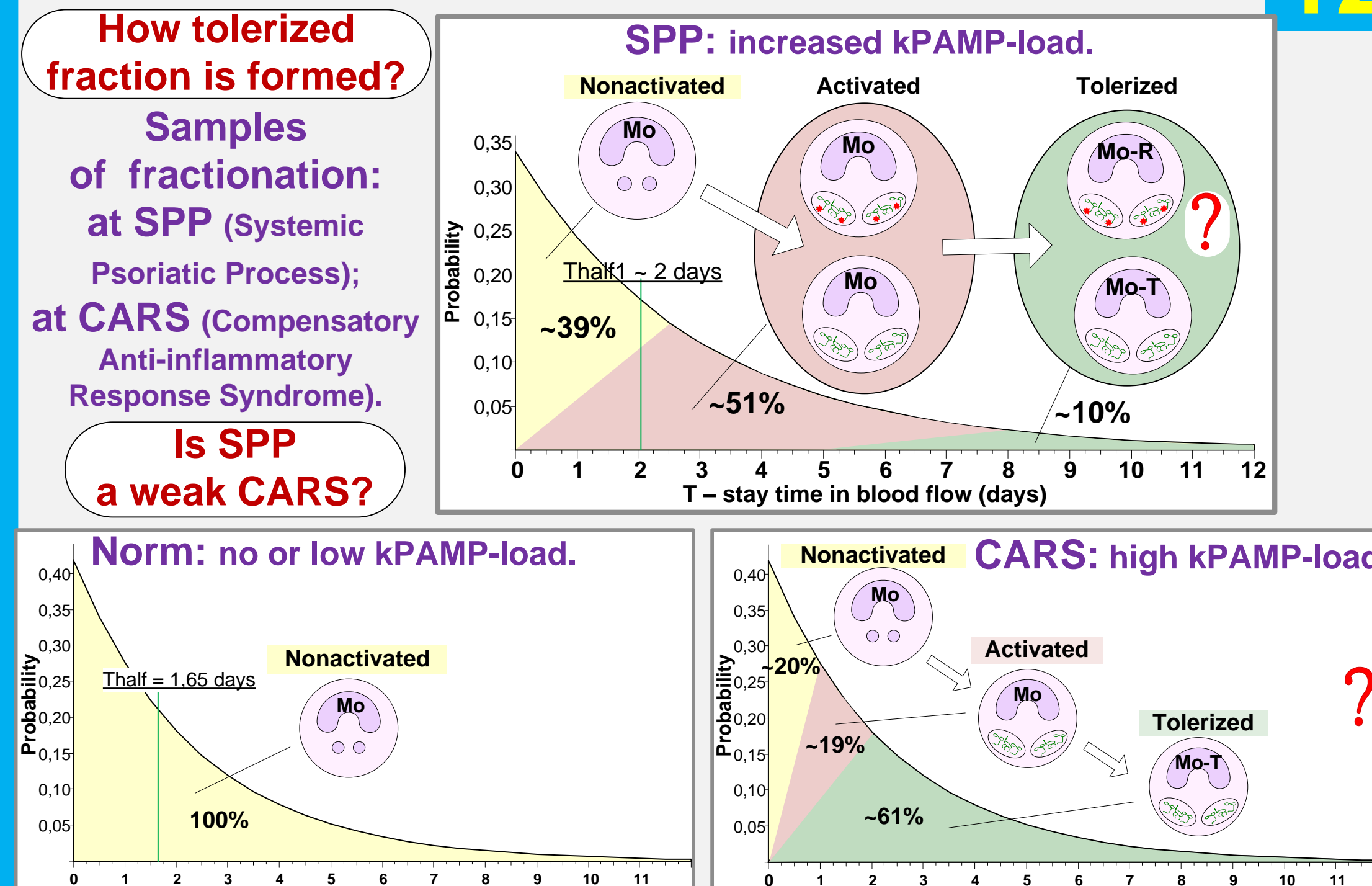
Property 2. They are kPAMP-carriers.

Ability to fast loss of tolerance (to be deprogrammed) under the influence of cytokines-deprogrammers IFN-gamma, GM-CSF and (indirectly) IL-12.

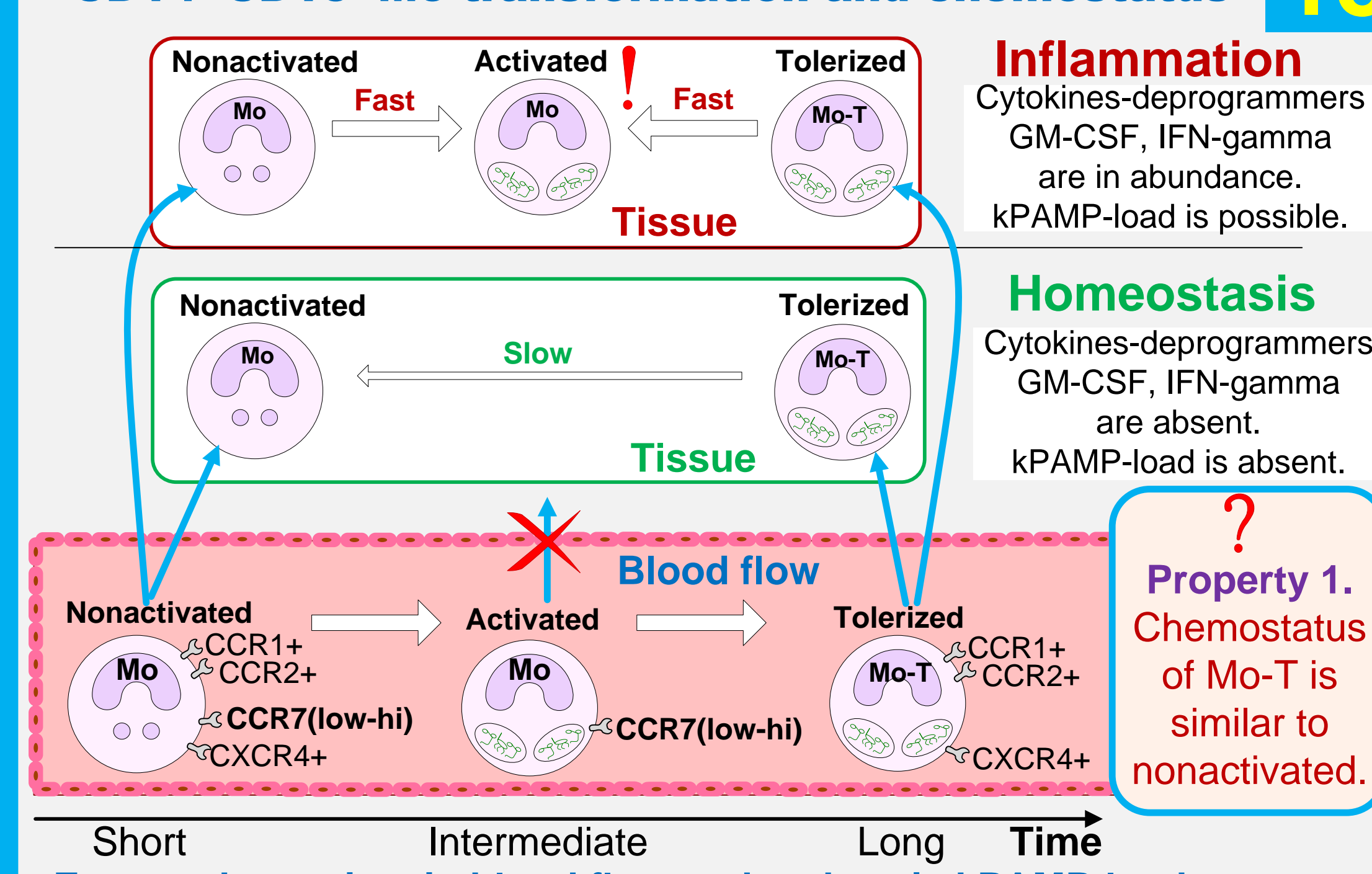
Property 1. Their chemostatuses (ranges of expressed chemokine receptors) are similar to nonactivated ones.

DC-T - yes  
Mo-T - ?

## Distribution of stay time of monocytes in blood flow



## CD14+CD16+Mo transformation and chemostatus



## Wanted!

Offence: Human body damages

Time: During and after damages made by others

Offence area: Skin and joints

Nicknames: Mo-T, DC-T (incl. Mo-R, DC-R)

Residence area: Blood flow of psoriatic persons

Special signs: Tolerized; kPAMP-carriers; Raised level of intracellular protein IRAK-M; (PG-Y)-carriers (Mo-R, DC-R only);

If you can help to find these blood phagocytes call police IFPA!