



FECAL MICROBIOTA TRANSPLANTATION

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Goloshchapov O.V.



05 июня, среда

**О.В. Голощاپов
2019
САНКТ-ПЕТЕРБУРГ**



10:00 – 10:40

My plan

1-fmt-story

2-fmt effects

3-fmt methods

4-fmt-indications

5-fmt results

6-fmt donors

7-fmt results

A-Microbiology

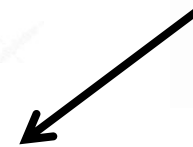
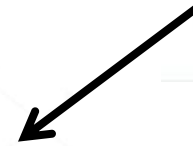
B-clinic

8-fmt contraindications

9-fmt complications

10-fmt laws

Your plan



Items: 1 to 20 of 7920

- [Successful treatment of fulminant Clostridium difficile infection with fecal bacteriotherapy.](#)

21. You DM, Franzos MA, Holman RP.
Ann Intern Med. 2008 Apr 15;148(8):632-3. No abstract available.
- [\[Feces culture successful therapy in Clostridium difficile diarrhea\].](#)

23. Jorup-Rönström C, Håkanson A, Persson AK, Midtvedt T, Norin E.
Lakartidningen. 2006 Nov 15-21;103(46):3603-5. Swedish. No abstract available.
- [Relapsing Clostridium difficile enterocolitis cured by rectal infusion of normal faeces.](#)

29. Schwan A, Sjölin S, Trottestam U, Aronsson B.
Scand J Infect Dis. 1984;16(2):211-5.
PMID: 6740251
- [Pseudomembranous enterocolitis. Further observations on the value of donor fecal enemata as an adjunct in the treatment of pseudomembranous enterocolitis.](#)

36. COLLINS DC.
Am J Proctol. 1960 Oct;2:389-91. No abstract available.
- [Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis.](#)

37. EISEMAN B, SILEN W, BASCOM GS, KAUVAR AJ.
Surgery. 1958 Nov;44(5):854-9. No abstract available.

- Article types
- Clinical Trial
- Review
- Customize ...
- Text availability

Format: Summary Sort by: Most Recent Per page: 20

Send to Filters: Manage Filters

Search results

Items: 1 to 20 of 1112

Sort by: Best match Most recent

<< First < Prev Page 1 of 56 Next > Last >>

The role of fecal microbiota transplantation in inflammatory bowel disease.

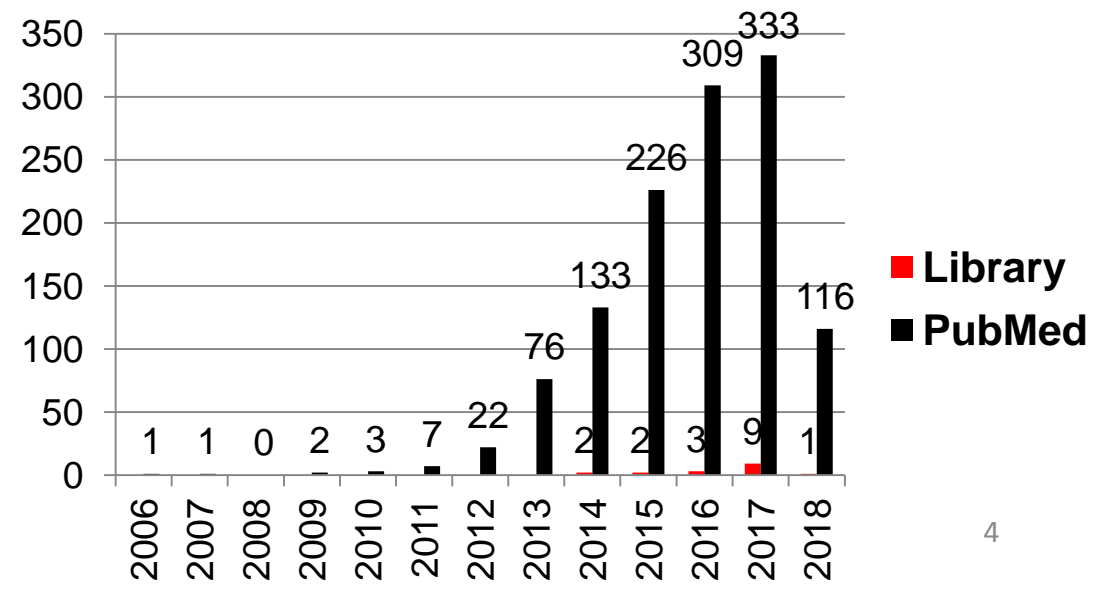
1. D'Odorico I, Di Bella S, Monticelli J, Giacobbe DR, Boldock E, Luzzati R. J Dig Dis. 2018 Apr 25. doi: 10.1111/1751-2980.12603. [Epub ahead of print] Review. PMID: 29696802

[Similar articles](#)

In vitro and in vivo assessment of intractintestinal bacteriotherapy in chronic kidney disease.

1112. Ranganathan N, Patel BG, Ranganathan P, Marczely J, Dheer R, Pechenyak B, Dunn SR, Verstraete W, Decroos K, Mehta R, Friedman EA. ASAIO J. 2006 Jan-Feb;52(1):70-9. PMID: 16436893

[Similar articles](#)



**“IS IT NOW FASHIONABLE ... !?
OR
NEW PROMISING DIRECTION IN MEDICINE ”**

OPENING OF CIRCULATION

ANESTHESIA IN SURGERY

X-RAYS

ANTIBIOTICS

CHEMICAL STRUCTURE OF DNA

**TRANSPLANTATION
FECAL
MICROBIOTES**

I or we -?

1,2 kg

70 kg

47 times

100 trillion microbes

> 37.2 trillion cell

3 times

8 million genes GIT
microbiome genome

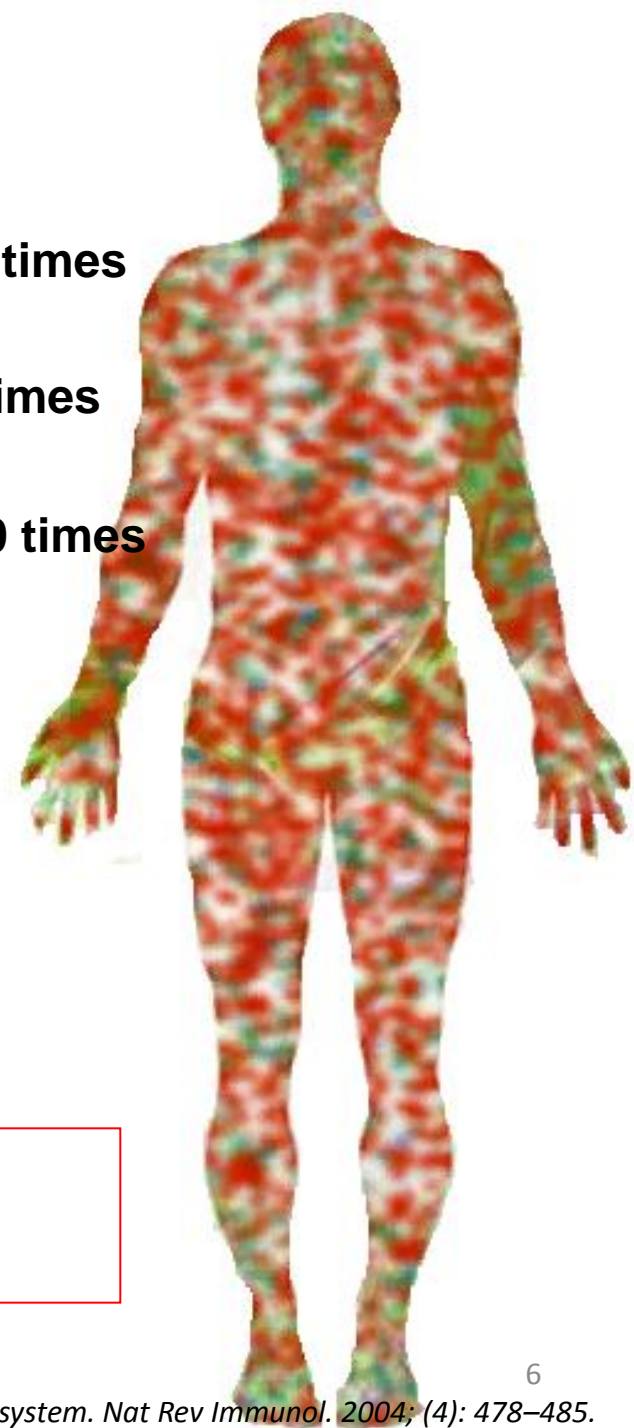
> 22 thousand genes
Genome human

150 times

1000-1150 species of bacteria - (160-10,000 species)

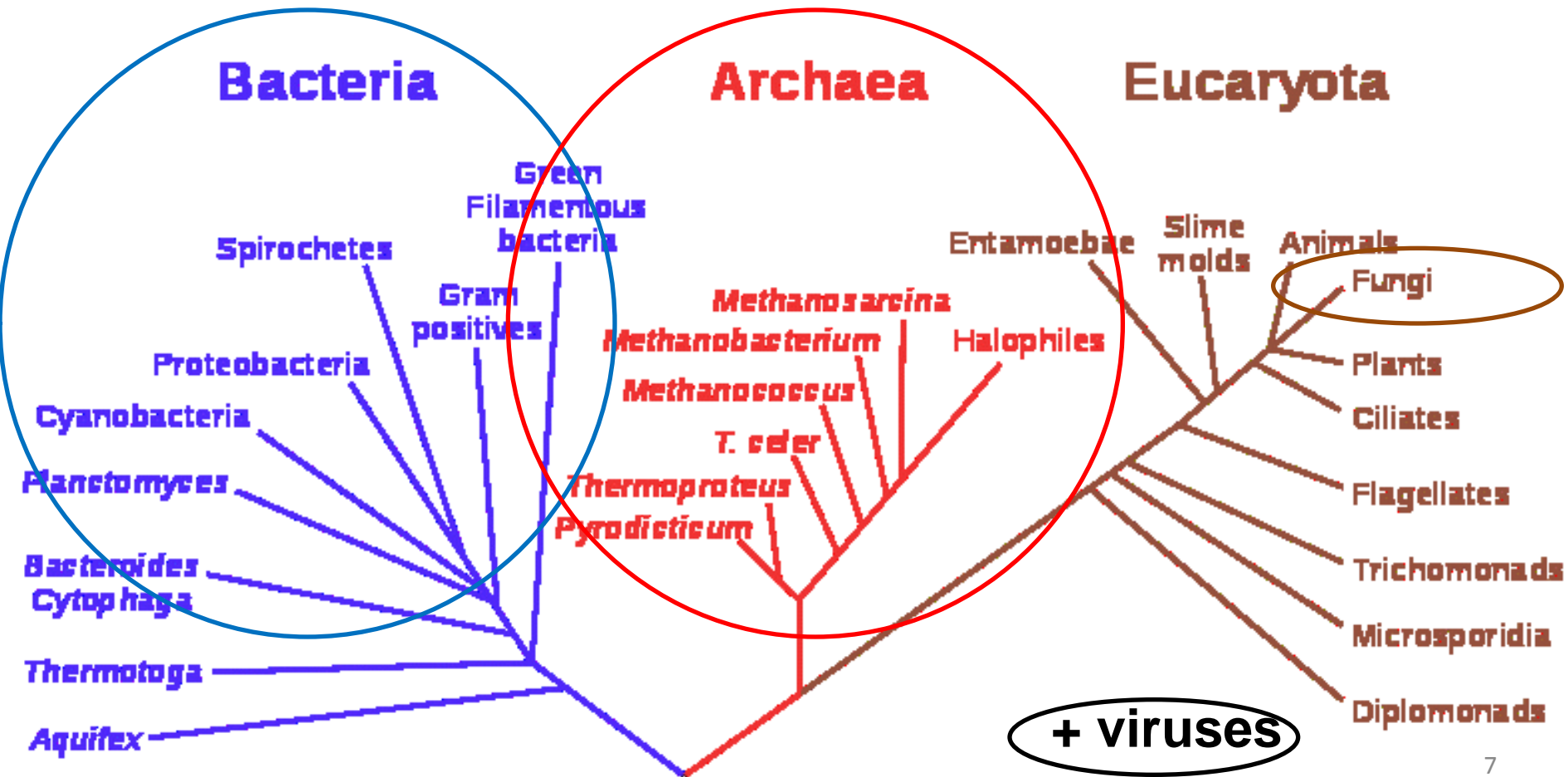
Quadrillion = viruses, fungi, parasites and archaea

**Superorganism - an organism
multiple organisms**



Phylogenetic tree

Domains: Bacteria, Archaea, Eukaryotes + Viruses



COMPOSITION OF HUMAN MICROBIOTS

Phylum	Class	Order	Genus	Gram stain
Firmicutes	Bacilli	Bacillales	<i>Gemella</i> <i>Staphylococcus</i>	+
		Lactobacillales	<i>Enterococcus</i> <i>Lactobacillus</i> <i>Streptococcus</i>	
	Clostridia	Clostridiales	<i>Blautia</i> <i>Clostridium</i> <i>Eubacterium</i> <i>Faecalibacterium</i> <i>Ruminococcus</i>	+
	Erysipelotrichia	Erysipelotrichiales	<i>Erysipelatoclostridium</i> <i>Holdemania</i>	+
Negativicutes	Selenomonadales	<i>Acidaminococcus</i> <i>Megasphaera</i> <i>Phascolarctobacterium</i> <i>Vulcanella</i>	-	
Bacteroidetes	Bacteroidia	Bacteroidales	<i>Bacteroides</i> <i>Prevotella</i>	-
Proteobacteria	Gamma proteobacteria	Enterobacteriales	<i>Escherichia</i> <i>Klebsiella</i>	-
Actinobacteria	Actinobacteria	Actinomycetales	<i>Actinomyces</i>	+
		Bifidobacteriales	<i>Bifidobacterium</i>	
Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	<i>Akkermansia</i>	-

> 90% of filotypes

Dominant species of bacteria

50%

50%

295 species

25 species

- *Faecalibacterium prausnitzii*
- *Eubacterium rectale*
- *Collinsella aerofaciens*
- *Clostridium clostridioforme*
- *Bacteroides vulgatus*
- *Anaerostipes hadrus*
- *Ruminococcus bromii*
- *Eubacterium hallii*
- *Blautia wexleri*
- *Bacteroides dorei*
- *Roseburia faecis*
- *Dorea longicatena*
- *Subdoligranulum variabile*
- *Bacteroides uniformis*
- *Ruminococcus obeum*
- *Bacteroides ovatus*
- *Blautia luti*
- *Parabacteroides distasonis*
- sp nov A2-166
- sp nov SR1/5
- *Lachnospira pectinoschiza*
- sp nov 80/3
- *Dialister invisus*
- *Roseburia inulinivorans*
- *Ruminococcus callidus*
- others

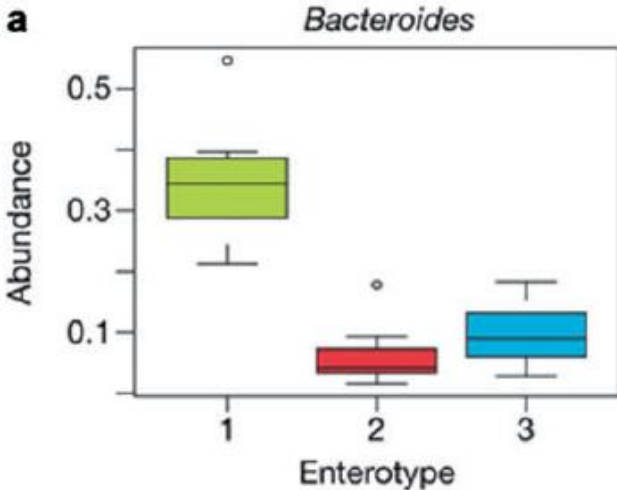
ENTEROTYPE

Enterotypes do not correlate with nationality, age, gender, body mass index

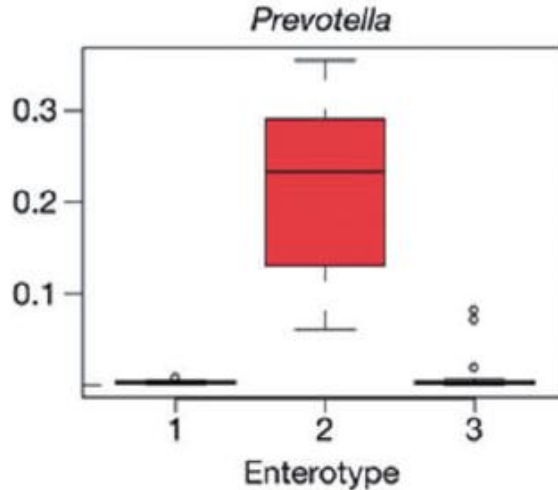
(America, Europe, Japan, Philippines)

Meat food

genus

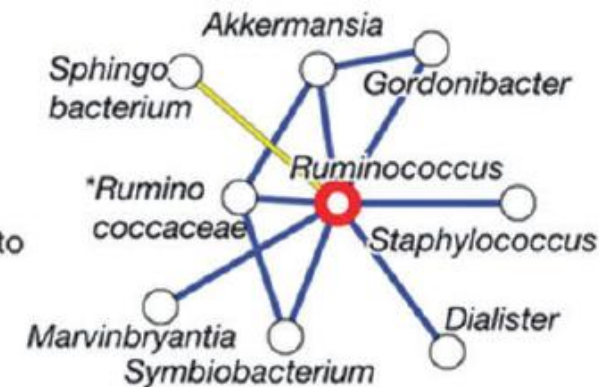
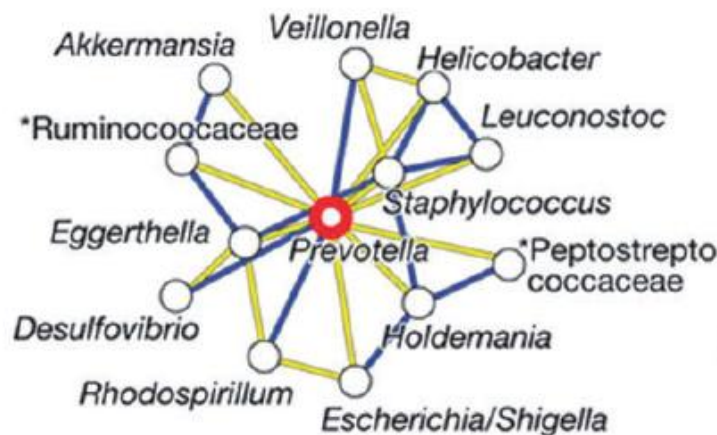
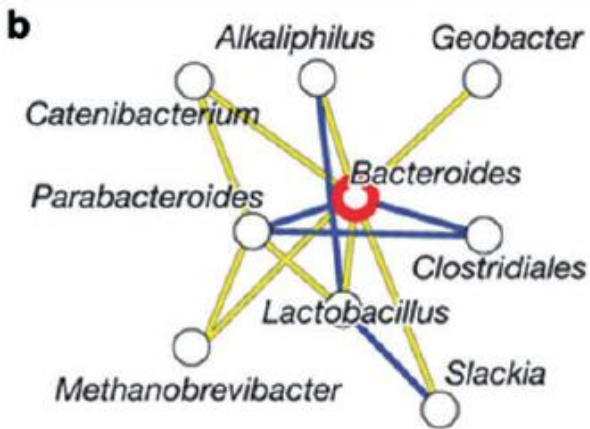
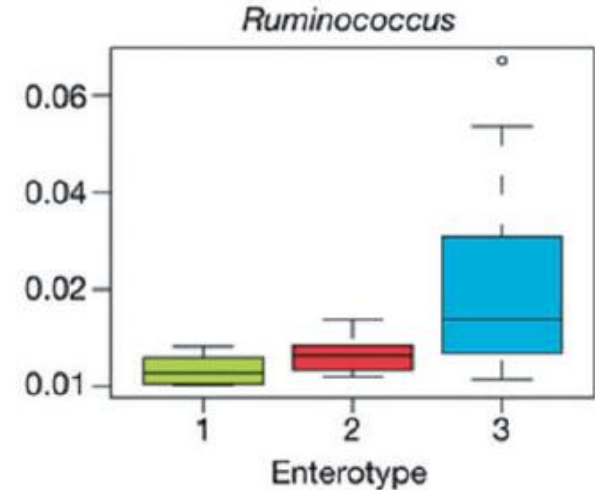


genus



Plant food

genus

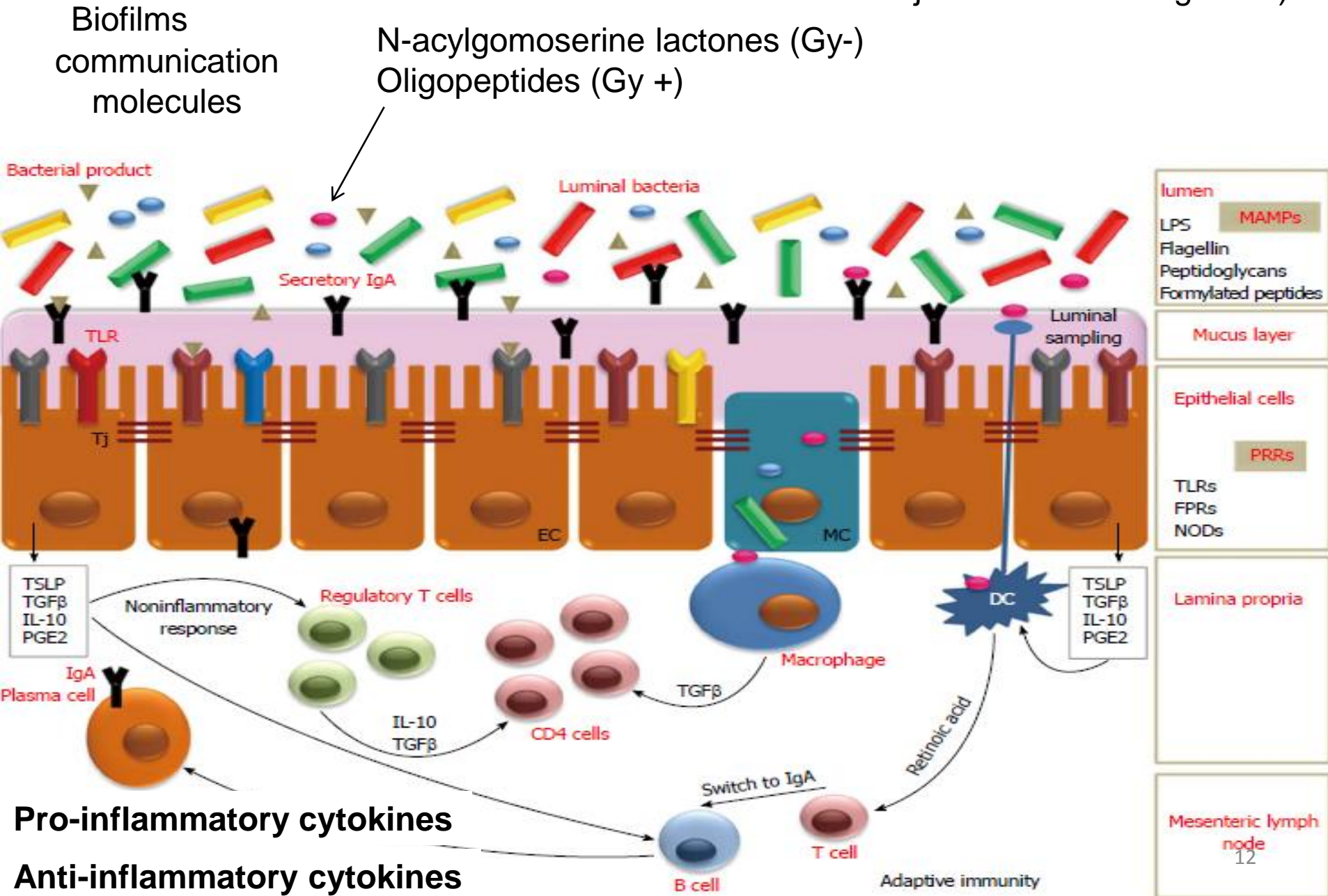




Blood type, fingerprints, iris and DNA barcodes, MICROBIOTA

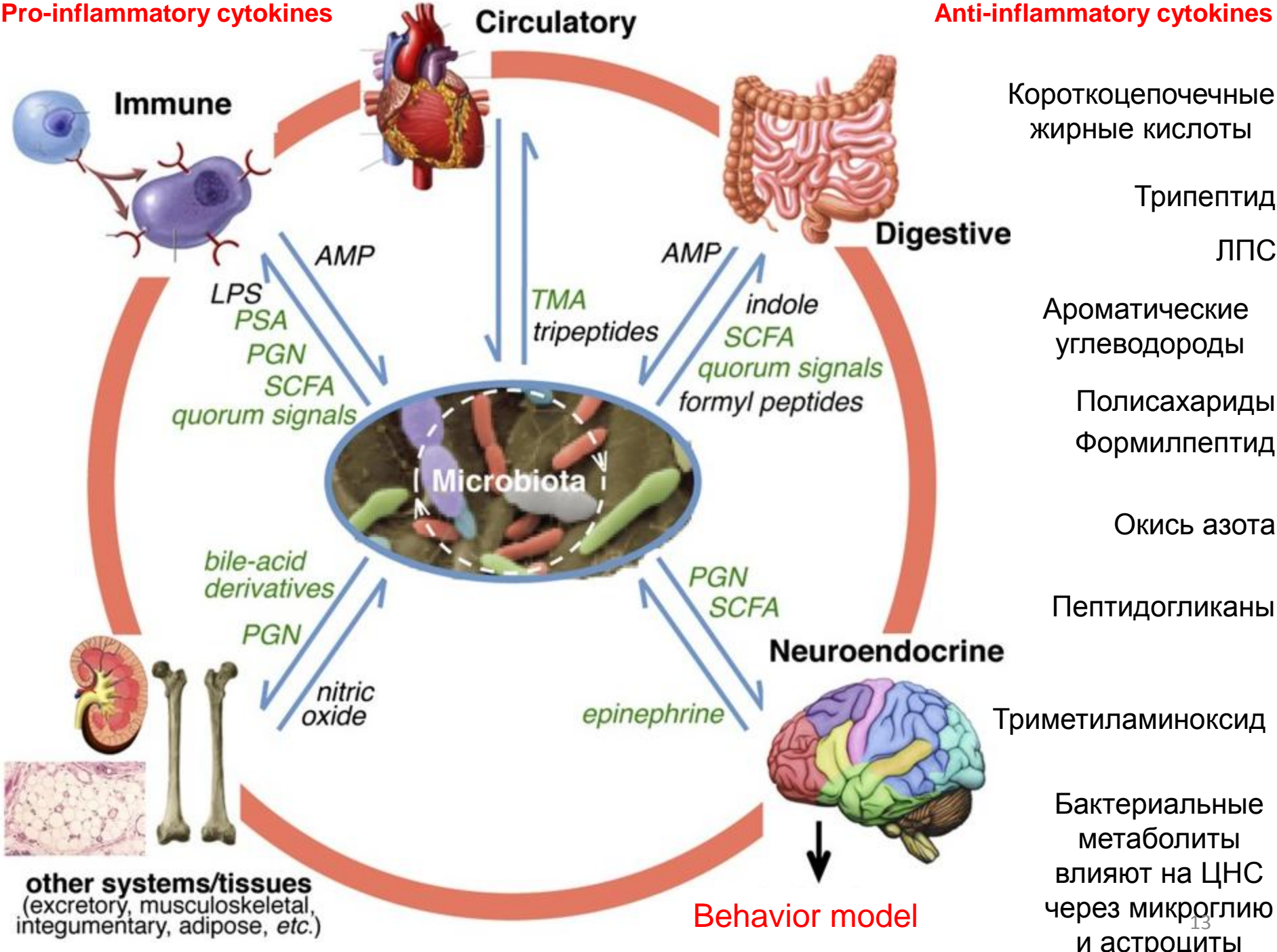
MICROBIOTA - BIOFILM ON EPITHELIUM SURFACE

«Das war ja toll!» That was great!«).



Pro-inflammatory cytokines

Anti-inflammatory cytokines



Indications for FMT

	Direction	Pub.
1	Therapy for Recurrent Infection Clostridium difficile	592
2	Inflammatory bowel disease, Crohn's disease, Nonspecific ulcerative colitis, antibiotic-associated diarrhea	133
3	Type II diabetes	60
4	Obesity, metabolic syndrome	92
5	Neuropsychiatric diseases (Parkinson's disease, multiple sclerosis, dystonia, myoclonus, chronic fatigue syndrome)	8
6	Autism	16
7	Bone marrow transplantation	13

FMT with recurrent *Clostridium difficile* infection

Efficiency

Systematic reviews and meta-analysis				
Author	Design	Patients	Mode of administration	Efficiency
Drekonja D et al. 2015	Generalized analysis of 2 randomized controlled trials	521	Options	85%
Kassam Z et al. 2013	Meta-analysis of 11 studies	273	Options	89%
Cohort studies				
O'Brien K et al. 2016	Multicenter cohort study on 482 health facilities	1406	Options	82%

FMT with recurrent *Clostridium difficile* infection

FMT / Other methods. Variants.

Author	Design	n	Mode of administration	Efficiency	Other	p
Kelly, C et al. 2015.	Multicenter, double-blind, randomized, FMT / placebo-controlled study	46	Colonoscopy	FMT - 91%	Auto-FMT (placebo) - 63%	
Lee, C et al. 2016	Double blind, randomized between frozen and fresh FT	232	Enema	Frozen FT 83.5%	Fresh FT - 85.1%	
Cammarota G et al. 2015	Randomized controlled trial between vancomycin and FMT	39	Colonoscopy	FMT - 90%	Vancomycin - 26%	p<.0001 99.9% CI
van Nood E et al. 2013	Randomized, controlled trial between FMT, Vanko. and Vanko. + intestinal lavage	43	Nazo-duodenal	FMT - 81%	Vancomycin - 31%	Vancomycin + Lavage - 23% p <.001

Inflammatory bowel disease,
Crohn's disease, Nonspecific ulcerative colitis, antibiotic-
associated diarrhea

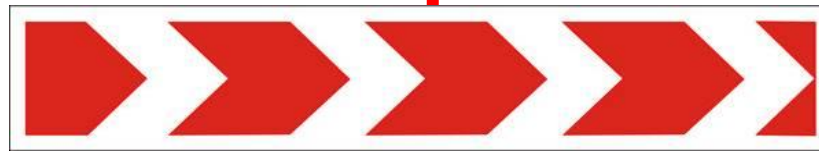
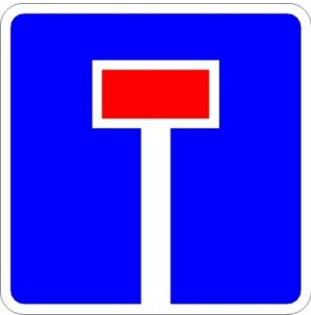
Nonspecific ulcerative colitis					
Paramsothy S et al. 2016	Double-blind, randomized, placebo-controlled study	81	Enema	Remission for 8 weeks.	FMT: 27%, Placebo - 8%, p=.02
Moayyedi P et al. 2015	Double-blind, randomized, placebo-controlled study	75	Enema	Remission for 7 weeks.	FMT: 24%, Water (placebo): 5%, p=.03; 95% CI
Rossen NG et al. 2015	Randomized, placebo-controlled trial	50	Nazo-duodenal	Remission for 4 weeks.	FMT:30%, Auto-FMT: 20%, p=.51

Bone marrow transplantation

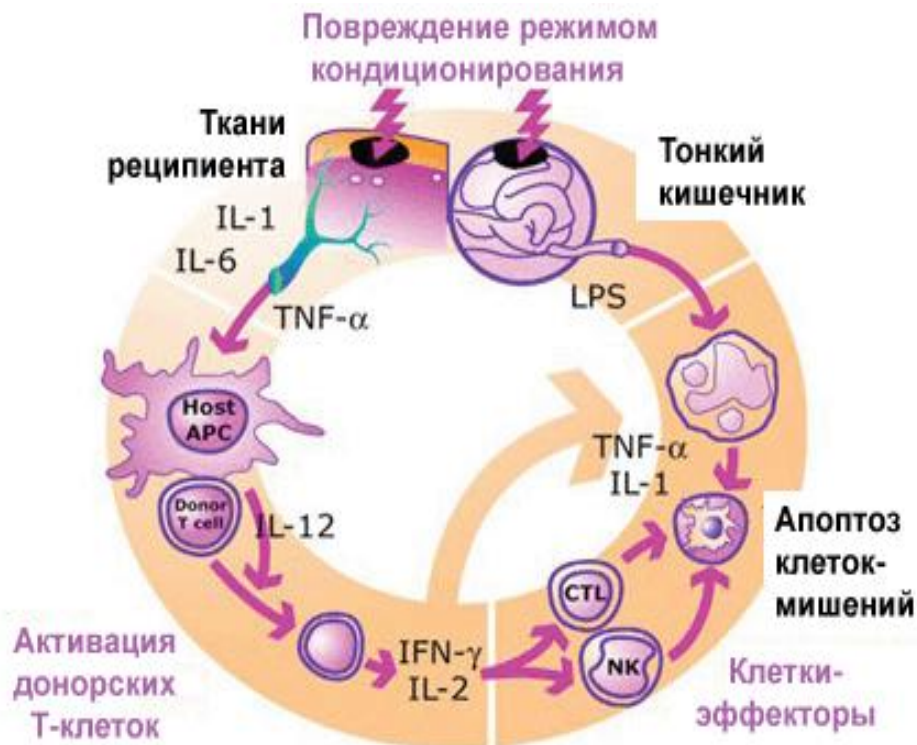


Decontamination
Isolation (boxes)
Laminar flows
Only RFP
Exclude sour-milk pr.
Sterile diet
Minimum of contacts
= STERILE INTELLIGENT =
STERILE PATIENT

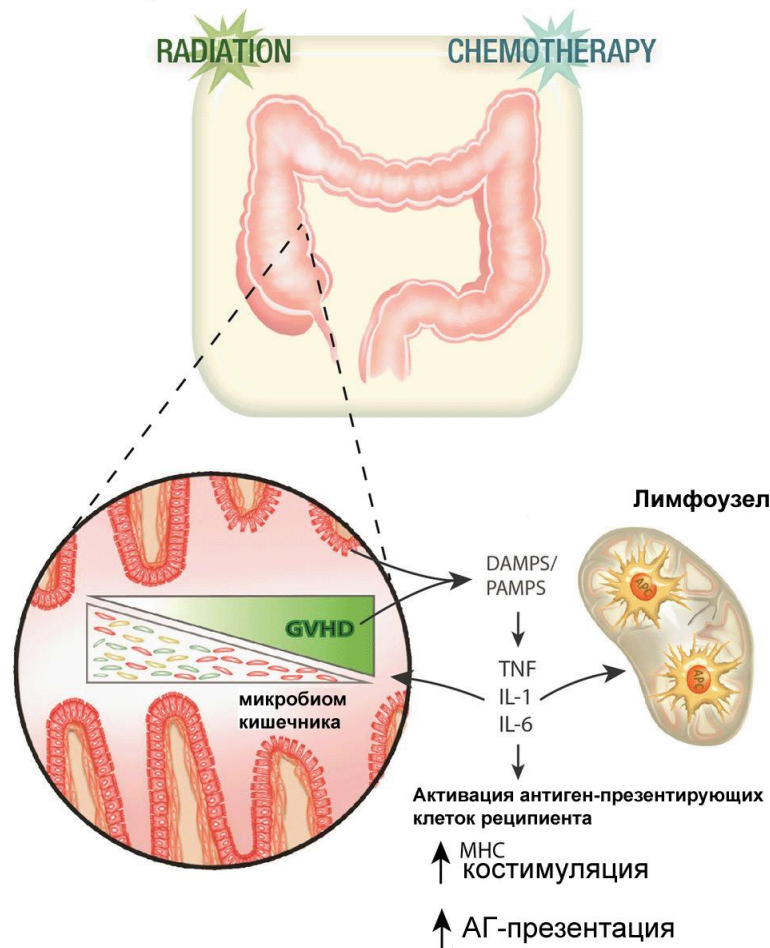
24 000 000 000



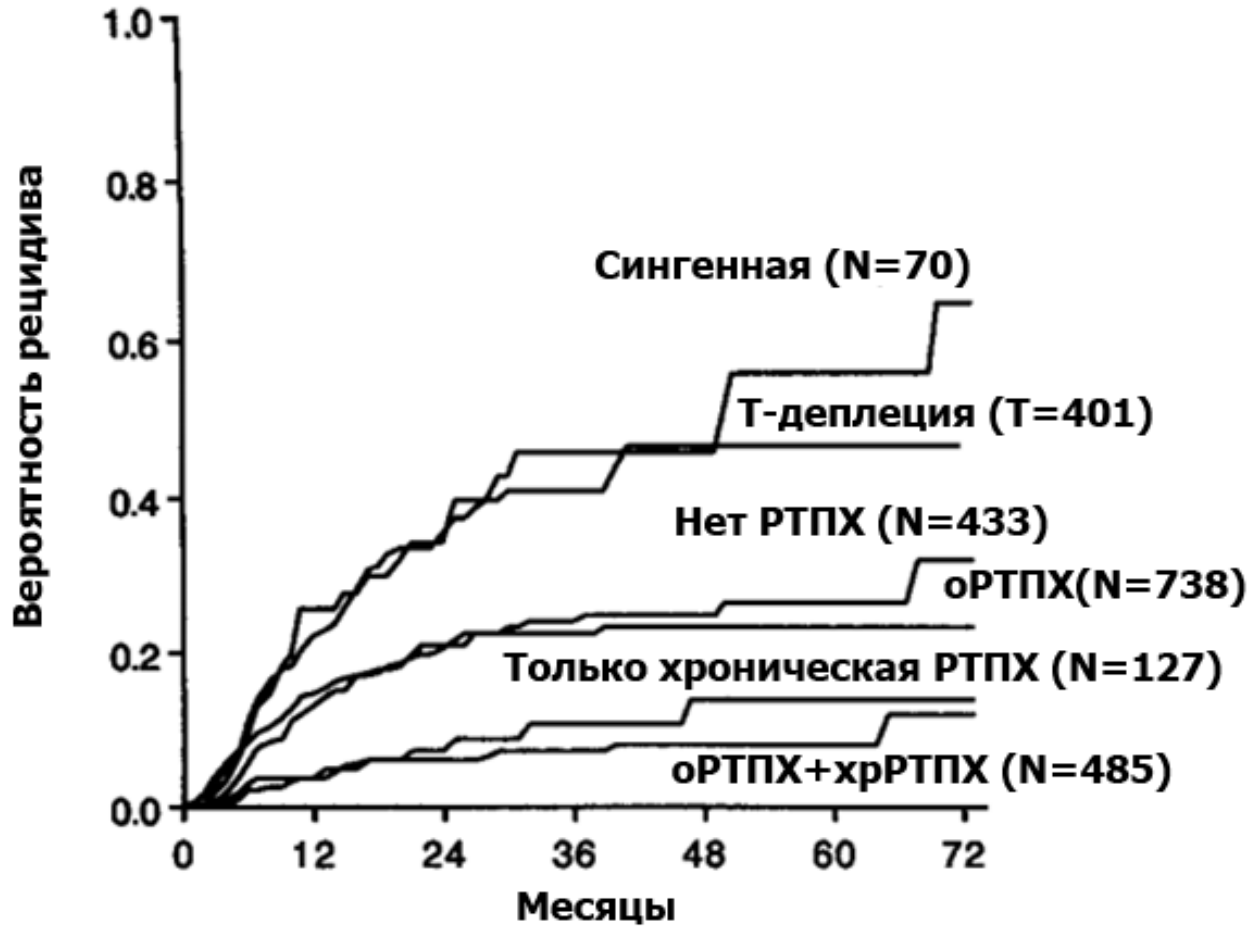
The pathogenesis of acute GVHD



Повреждение тканей кондиционированием

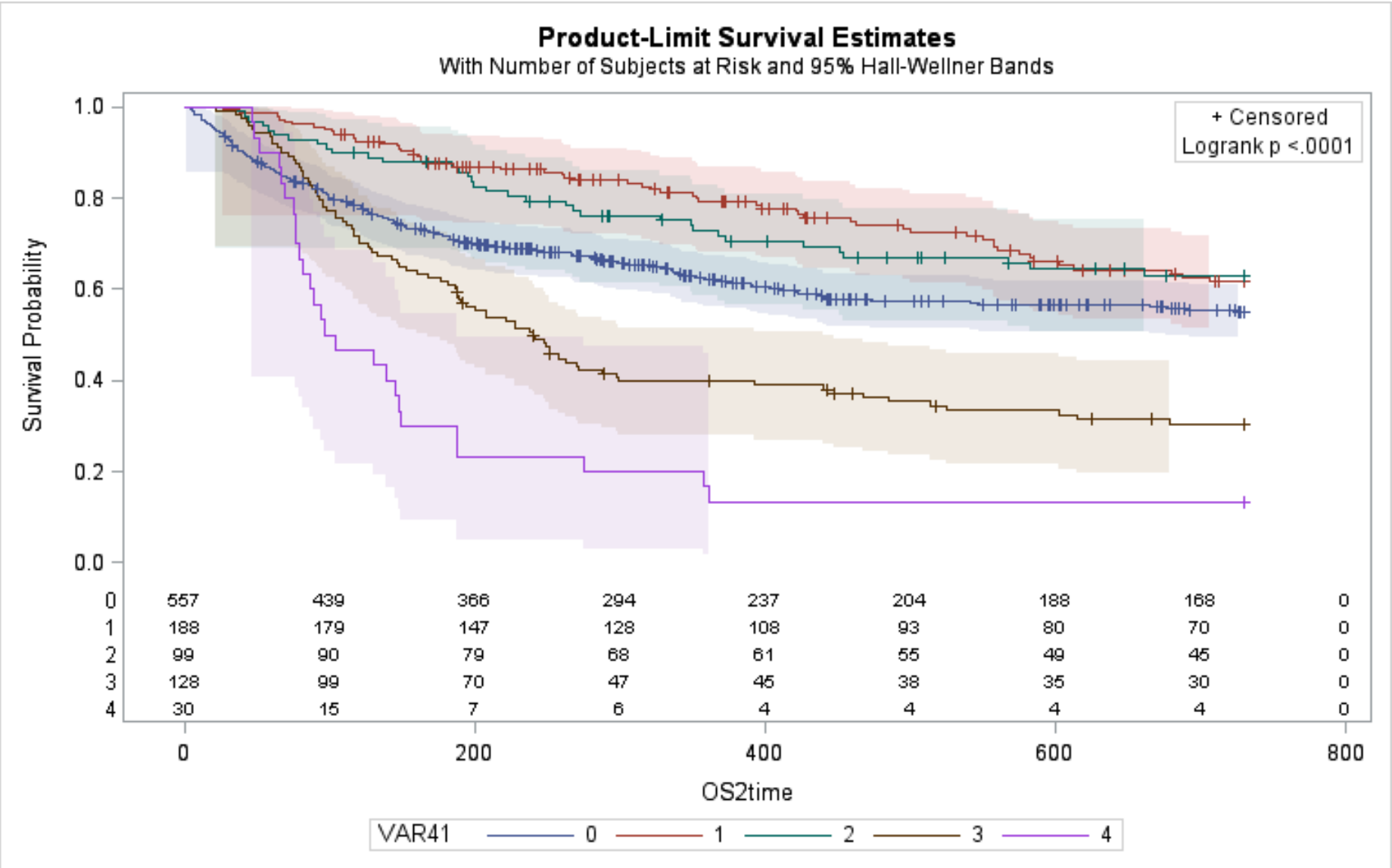


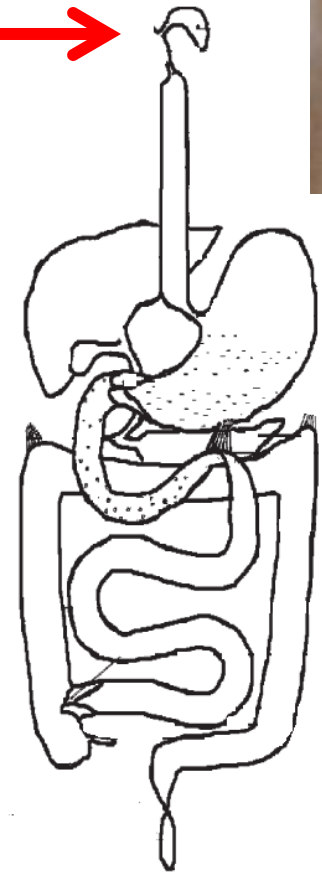
ALLO- HSCT reduces the likelihood of recurrence due to the reaction "graft against leukemia"

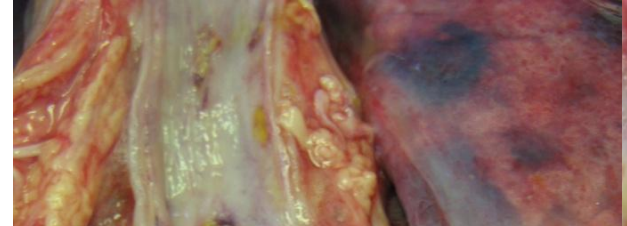
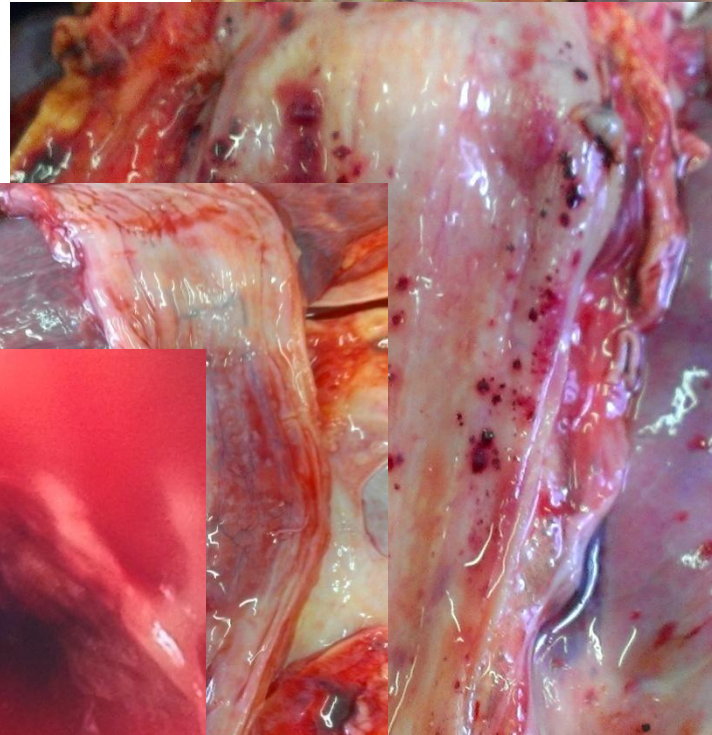
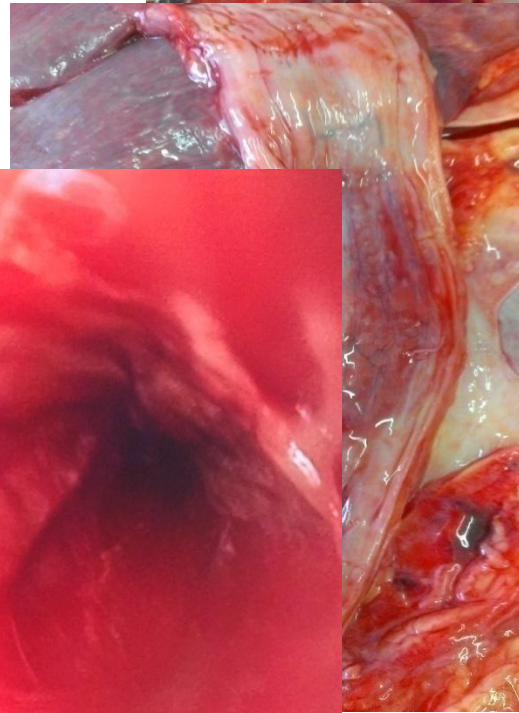
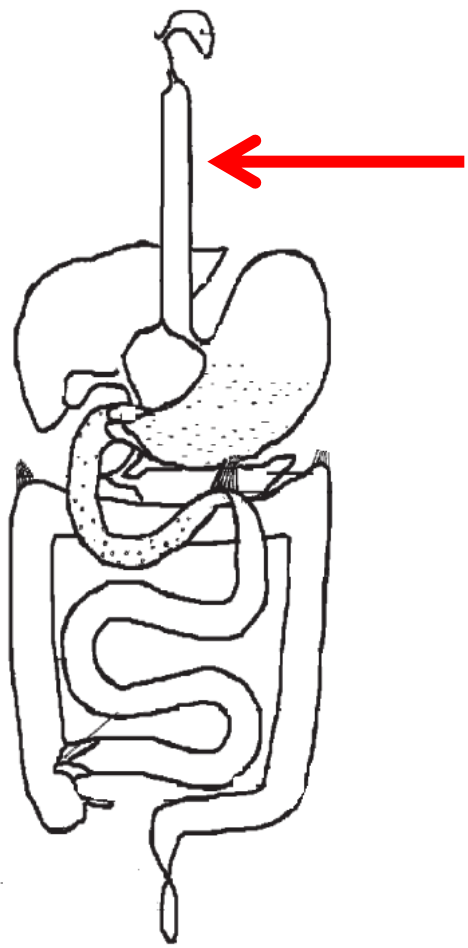


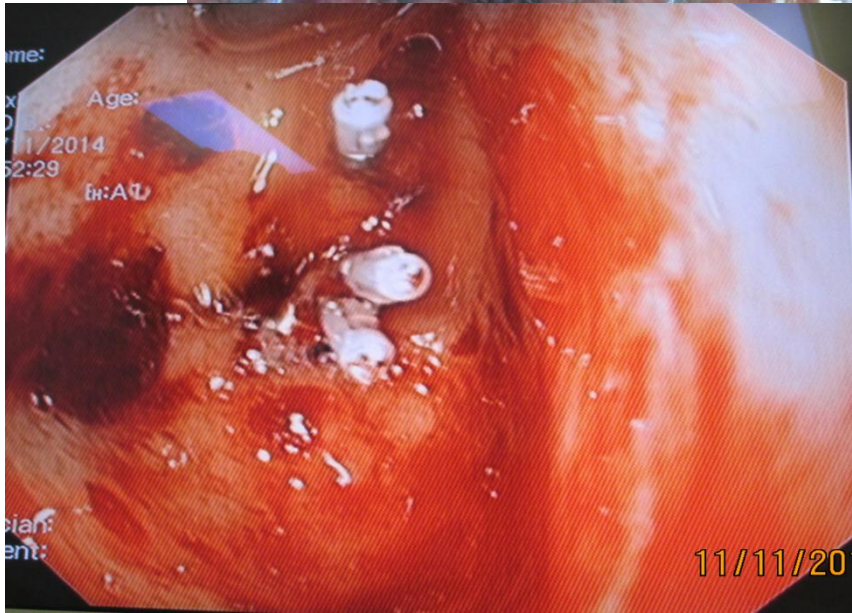
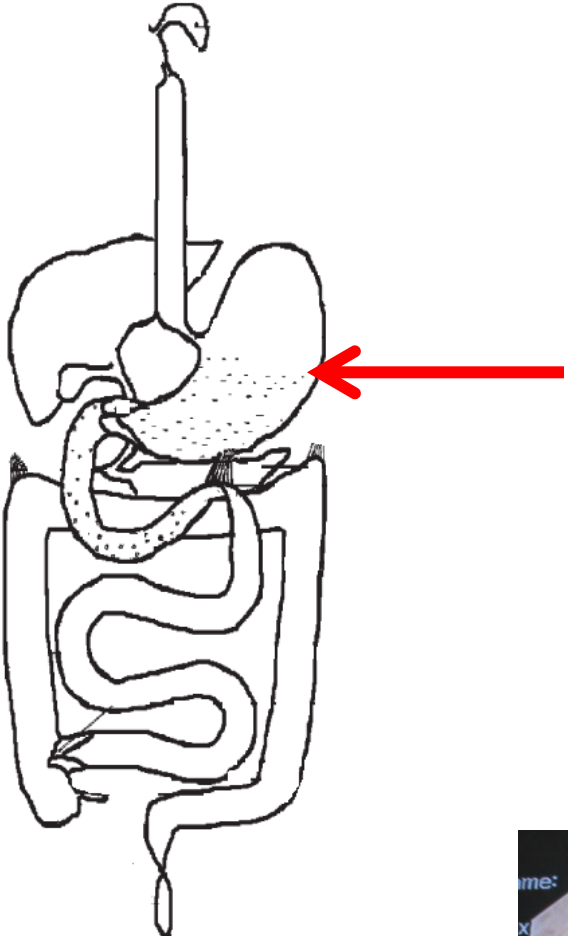
Вероятность рецидива при острых лейкозах в зависимости от типа трансплантации и наличия РТПХ

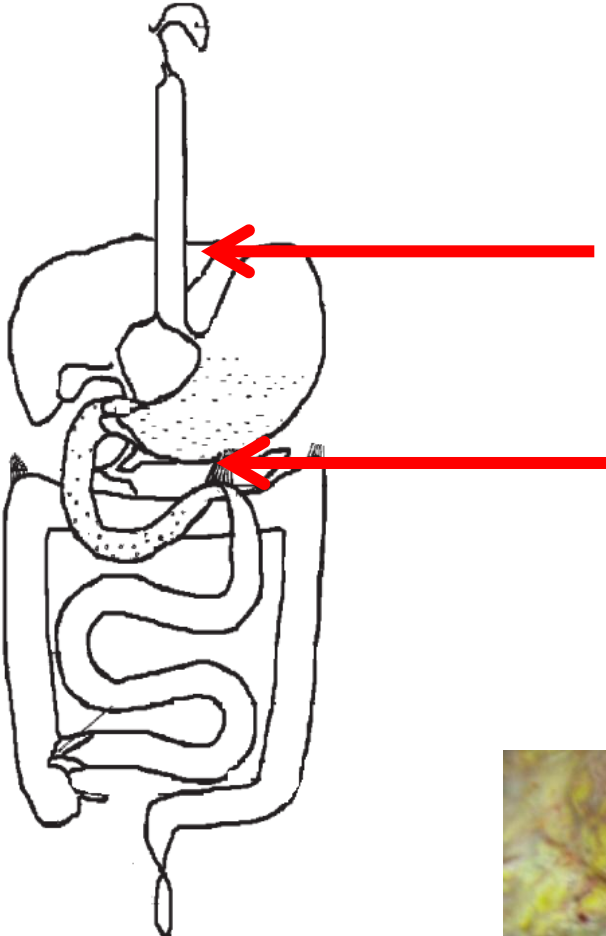
Survival of patients depending on the severity of GVHD

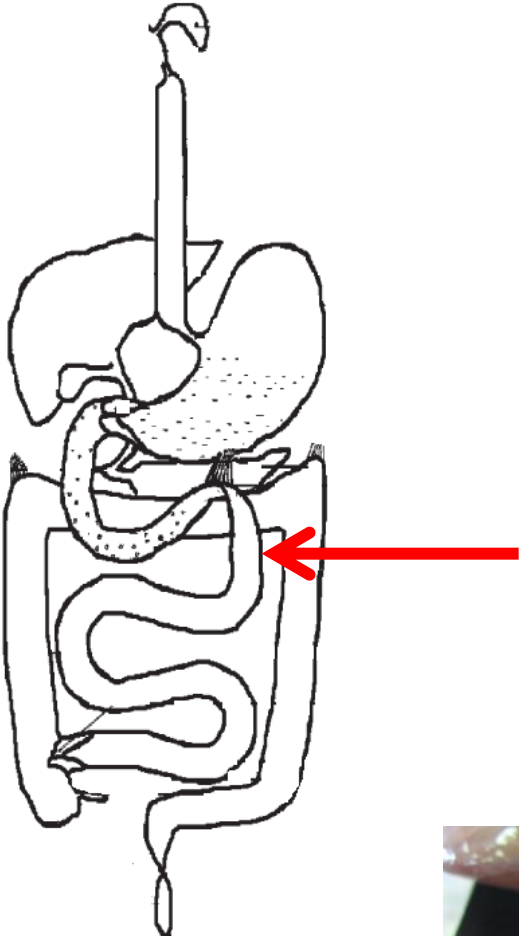


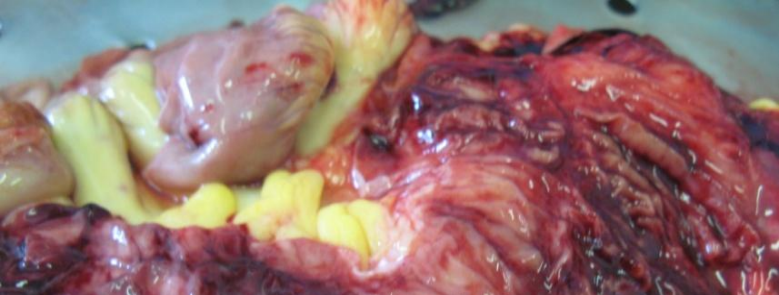
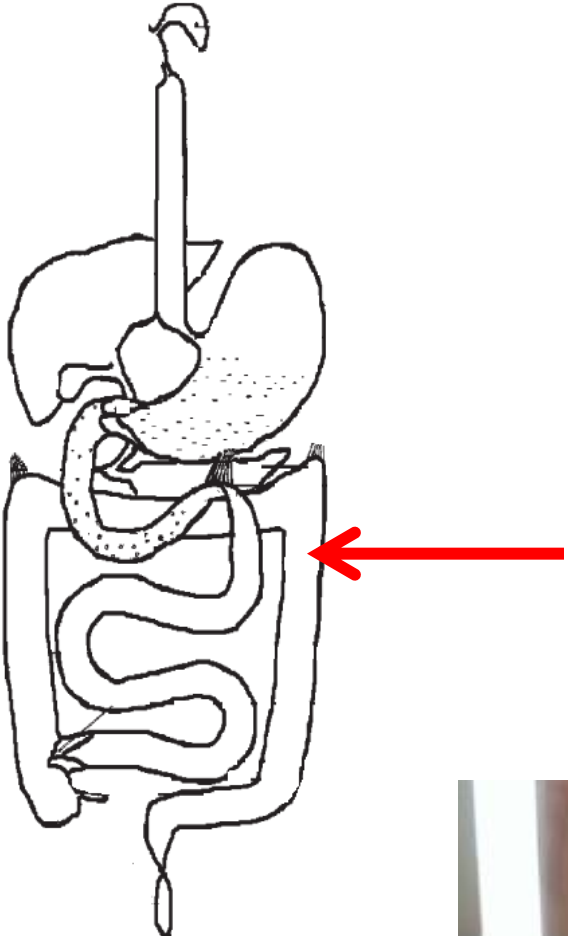


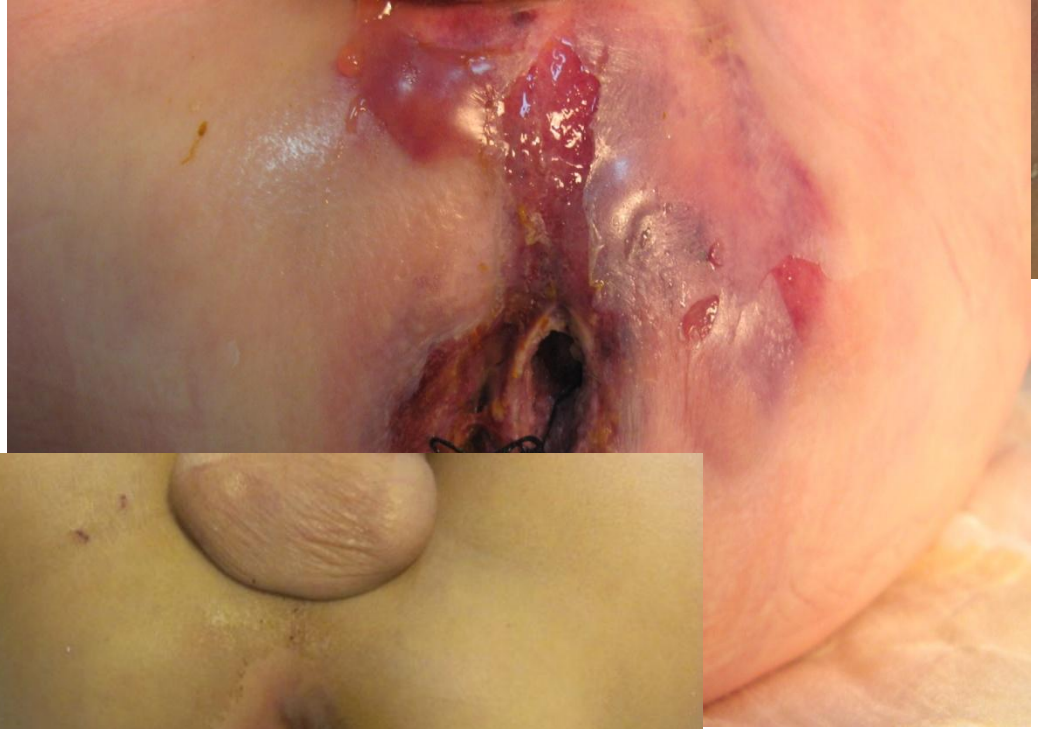
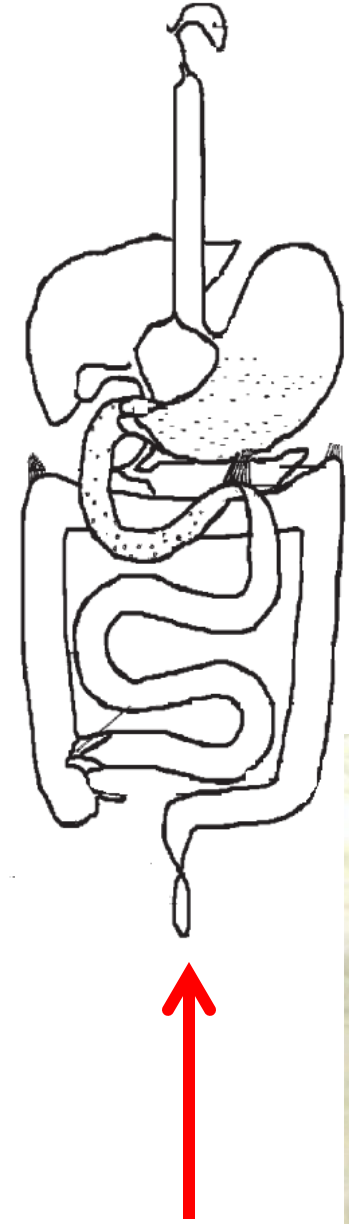




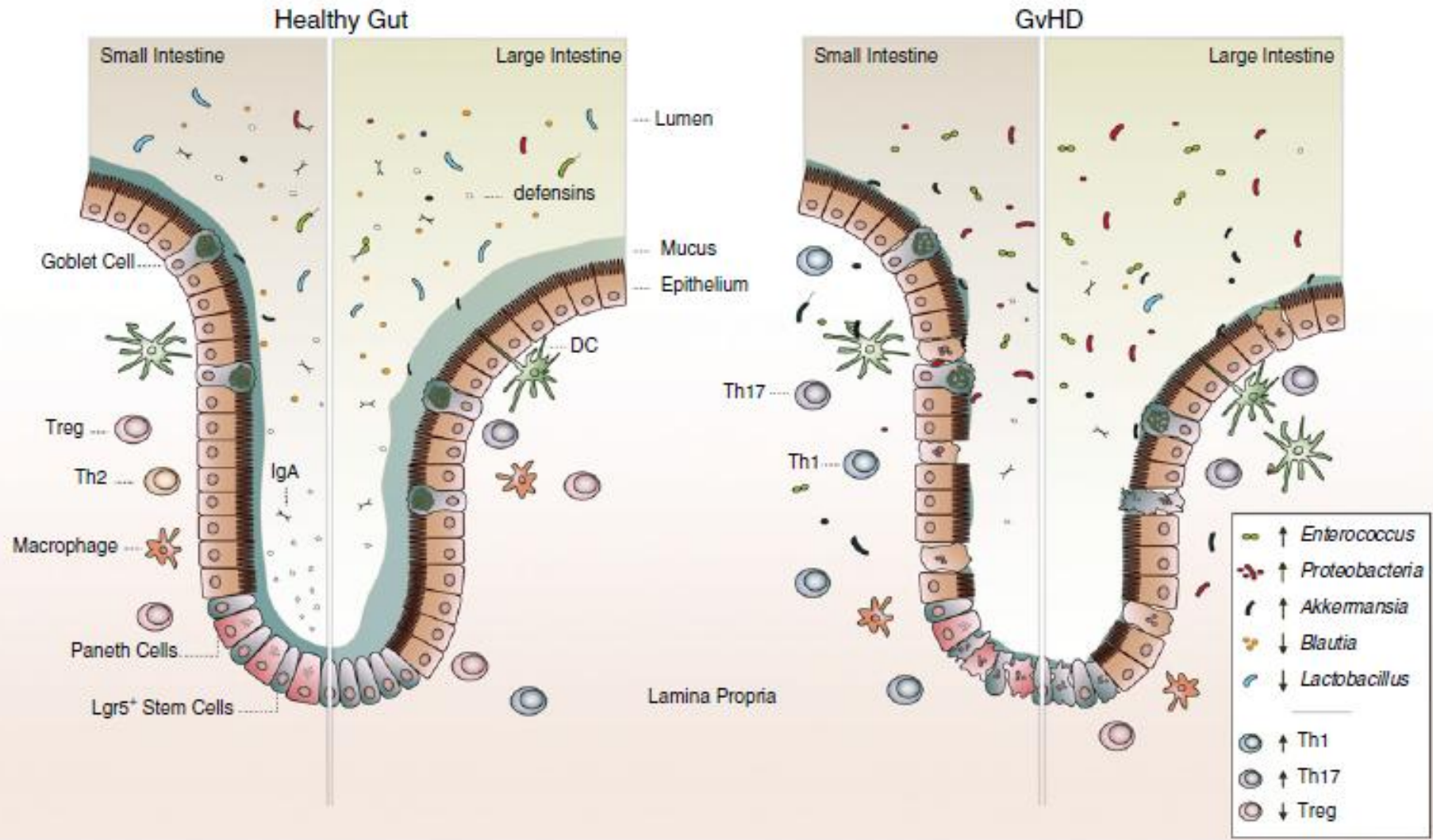






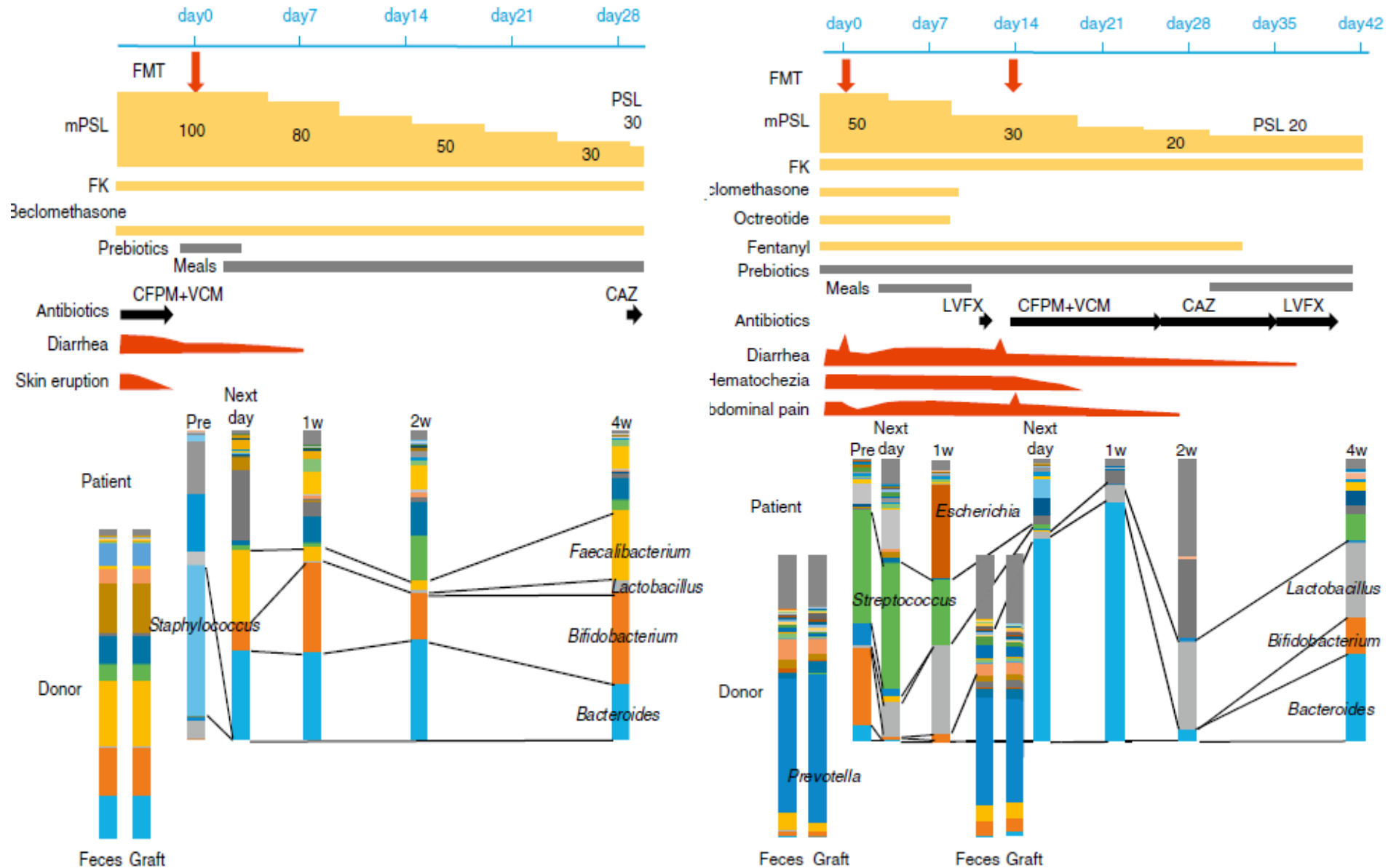


Hematopoietic stem cell transplantation (GVHD)



The intestinal microbiota in allogeneic hematopoietic cell transplant and graft-versus-host disease Anna Staffas et al. BLOOD, 23 FEBRUARY 2017 x VOLUME 129, NUMBER 8

Hematopoietic stem cell transplantation (GVHD)



Blood. 2016 Oct 20; 128(16): 2083–2088. Fecal microbiota transplantation for patients with steroid-resistant acute graft-versus-host disease of the gut Kazuhiko Kakihana et al

«Treatment of children and adults with inflammatory and infectious lesions of gastrointestinal tract after allogeneic hematopoietic stem cell transplantation with transplantation of normal human fecal microbiota »

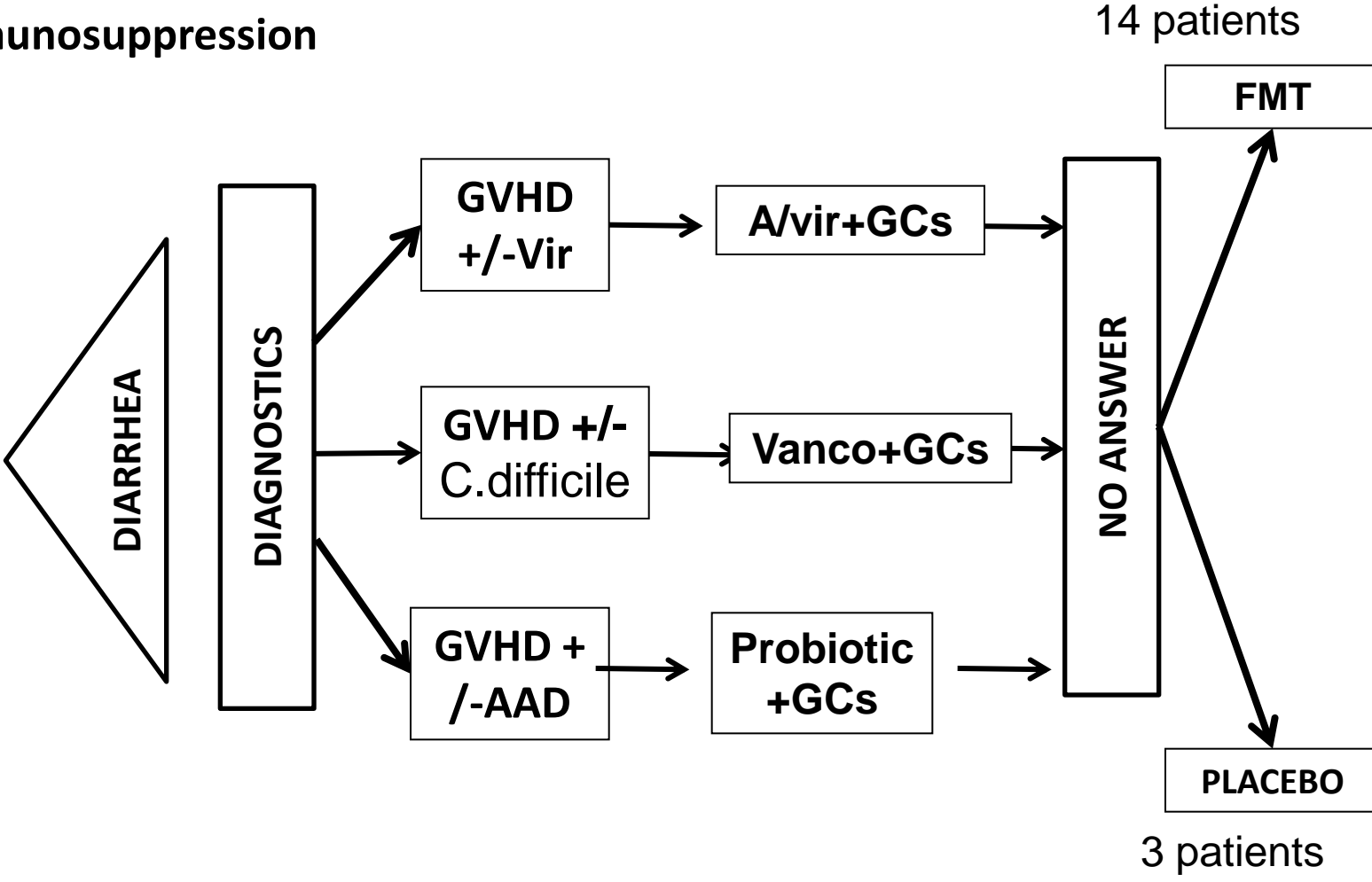
Objectives: To improve overall survival in patients with malignancy and hematological diseases after HSCT with multiresistant bacterial infection, *Clostridium difficile* infection, idiopathic antibiotic-associated diarrhea and acute and chronic GVHD with gastrointestinal lesions, by including fecal microbiota transplantation to complex therapy plan.

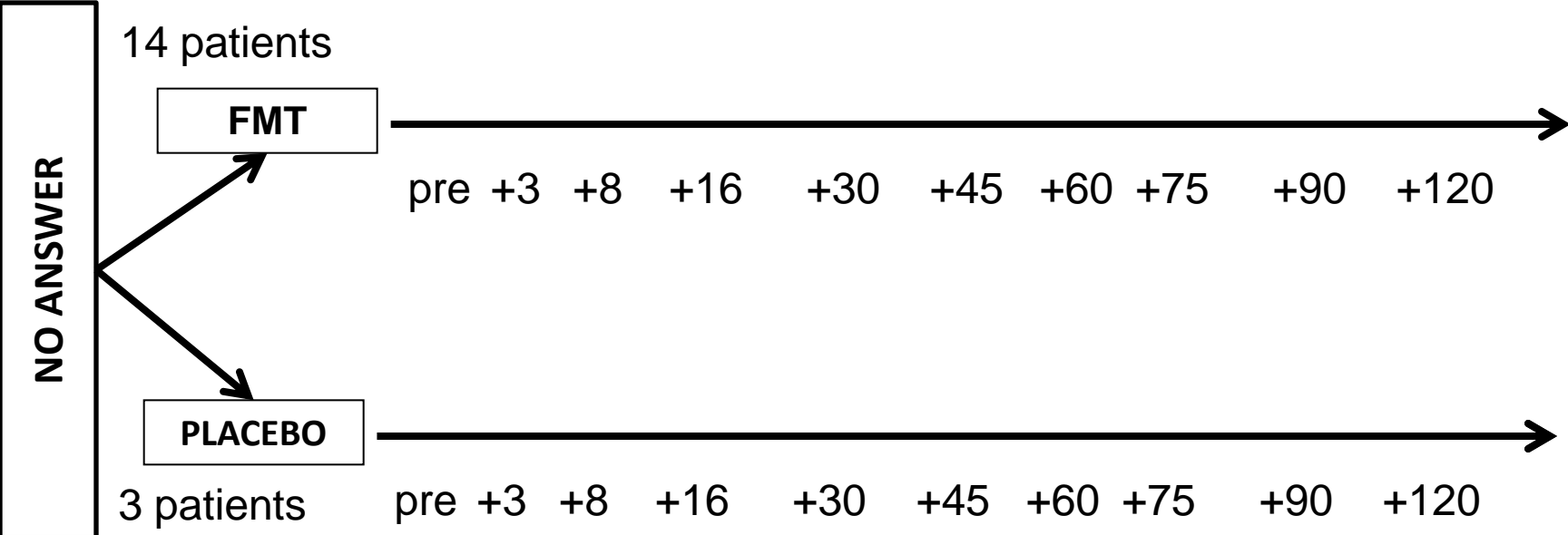
Materials and methods for microbiota analysis:

- 1-Real-time PCR of the main groups of intestinal microorganisms (“Kolonoflor-16”)
- 2-16S-RNA sequencing (Illumina MiSeq)

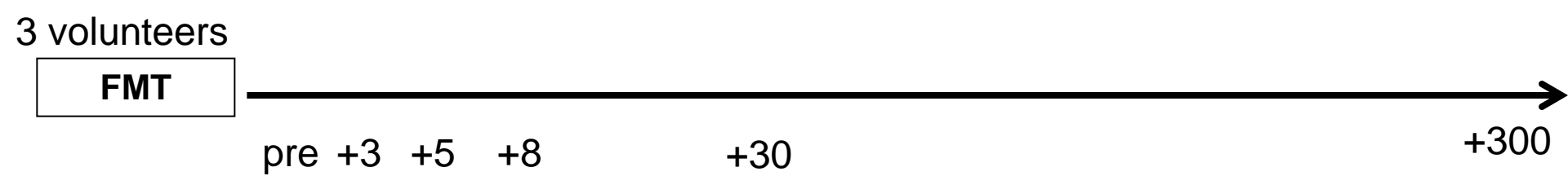
Conditioning
Decontamination
Antibiotics
Immunosuppression
Diet

HSCT





No	year	sex	Diagnosis	Donor BM	Cond.	Proph.GVHD	Therapy GVHD	Donor FT	Donor FT (sex)	Donor (year)	Donor char.	Treatment
1	10 M	M	LL	haplo	ATG,Tx,Sir	Flu+Treo	GCs, Ruxo	plac	plac	plac	plac	EGD
2	39	f	CML	haplo	Flu+Bu	Cy+Tx+MMF	Sir+GCs+Ruxo	plac	plac	plac	plac	EGD
3	46	f	HXII	2-haplo	Flu+Cyc	Cy+MMF	CsA+Etanersept	plac	plac	plac	plac	EGD



No	year	sex	3 volunteers				Donor FT	Donor FT (sex)	Donor (year)	Donor char.	Management
1	46	M	volunteer - 1				u.d.	f	33	no	Caps.
2	36	M	volunteer - 2				u.d.	f	33	no	Caps.
3	26	f	volunteer - 3				u.d.	f	33	no	Caps.

Patient characteristics

No	Year	Sex	Diagnosis	Donor BM	Cond.	Proph.GVHD	Therapy GVHD
1	10	f	LL	haplo	Flu+Mel	Sir+Tx+MMF	GCs+Etanersept+Ruxo+Mes. cells, Fotoph.
2	28	m	AML	haplo	Flu+Bu	CyC+Tx+MMF	GCs+Ruxo
3	16	m	LL	haplo	Flu+Bu	CyC+Tx+Sir	GCs+Etanersept+Ruxo
4	42	m	AML	a.u.	Flu+Mel	CyC+Tx+MMF	GCs+Ruxo
5	3	m	Beta-thalassemia	haplo	Flu+Bu	CyC+Tx+MMF	GCs+Ruxo
6	24	m	AML	a.u.	Flu+Bu	Bend.	GCs+Ruxo
7	32	m	CML	a.u.	Flu+Bu	CyC	GCs+Tx+Etanersept+Ruxo
8	36	m	AML	a.u.	Flu+Bu	Bend.	GCs+Ruxo+Sir
9	45	m	MDS	a.u.	Flu+Bu	Tx+MMF+ATG	GCs+Ruxo+Sir
10	35	f	HL	haplo	Flu+Bend	CyC+Tx+MMF	GCs+Etanersept
11	40	m	CML	a.r.	Flu+Bu	CyC	GCs
12	3	f	MDS	haplo	Flu+Mel	ATGAM	GCs+Ruxo.
13	6	f	An. Fan.	a.u.	Flu+Cyc	ATG+CsA+MMF	GCs+Ruxo+Sir
14	23	f	LL	haplo	Flu+Bu	CyC+Tx	GCs+Sir

<i>min</i>	3	<i>f</i>	5	haplo	7	Diagnosis	LL	AML	Beta-thalassemia	CML	MDS	HL	An. Fan.
<i>med</i>	25	<i>m</i>	9	<i>a.u.</i>	6	<i>n</i>	3	4	1	2	2	1	1
<i>max</i>	45			<i>a.r.</i>	1	%	21,4	28,6	7,1	14,3	14,3	7,1	7,1

Fecal microbiota type and donor characteristics

No	FN	Donor FT	Donor FT (sex)	Donor FT (year)	Donor FT (diet)	Treatment	Single dose (ml/gr) EGD/caps.	Single dose (ml/gr) CS
1	H.B.	mother	f	33	no	EGD+CS	80	150
2	П.А.	brother	m	33	no	EGD+CS	100	150
3	М.Д.	father	m	40	no	CS	0	150
4	С.А.	u.d.	m	36	vegan	EGD+CS	100	150
5	А.Н.	father	m	34	no	EGD+CS	20	50
6	В.А.	u.d.	f	31	no	Caps.	22	0
7	Т.Д.	u.d.	f	31	no	Caps.	22	0
8	Ш.А.	u.d.	f	32	no	Caps.	22	0
9	К.К.	u.d.	m	16	no	NIS	400	0
10	Ф.И.	u.d.	f	32	no	Caps.	22	0
11	Ф.А.	u.d.	f	32	no	Caps.	22	0
12	М.А.	u.d.	f	33	no	NIS	100	0
13	П.М.	father	m	36	no	NIS	90	0
14	Л.А.	u.d.	f	23	no	Caps.	22	0

<i>min</i>	16	<i>f</i>	8	related	5	Manag	Caps.	EGD	CS	EGD+CS	NIS	Single dose (ml/gr) EGD/caps	Single dose (ml/gr) CS
<i>med</i>	31,5	<i>m</i>	6	unrelated	9	n	6	1	1	3	3	2,5-8 ml/kg	6,2-12,5 ml/kg
<i>max</i>	40					%	42,8	7,1	7,1	21,4	21,4		

Before FMT

		MEC	Before FMT (10 d.) med.					Before FMT (0-3)					
№	FN	Diarrhea	Frequency of stool	Stool volume	Stool volume per 1 kg	Blood in the stool	Blood in the stool	Mucus in the stool	Nausea	Vomiting	Appetite	Pain	
1	H.B.	6	12,3	615	47,3	Yes	3	3	3	3	0	3	
2	П.А.	1	9	800	11,8	Blood.	3	3	3	2	1	2	
3	М.Д.	Excluded from the study - violation of technology FMT											
4	С.А.	Excluded from the study - violation of technology FMT											
5	А.Н.	3	9	458	31,6	Yes	3	3	3	3	0	3	
6	В.А.	2	10,5	1896	30,1	Blood	3	3	3	3	0	3	
7	Т.Д.	Excluded from the study - SIRS											
8	Ш.А.	1	6,2	160	2,2	Yes	1	3	0	0	0	2	
9	К.К.	4	31,3	2693	33,7	Blood	3	3	0	2	0	3	
10	Ф.И.	2	5,7	3128	50,5	No	0	0	0	0	3	1	
11	Ф.А.	нет	2	200	2,8	No	0	0	1	0	2	0	
12	М.А.		15	1022	68,1	Blood	3	3	2	2	0	3	
13	П.М.	1	9	731	40,6	Blood	3	3	2	2	0	3	
14	Л.А.	1	7	966	17,9	Yes	1	2	0	0	1	2	

№	Diarrhea	Frequency of stool	Stool volume	Stool volume per 1 kg	Blood in the stool	Blood in the stool	Mucus in the stool	Nausea	Vomiting	Appetite	Pain
<i>med</i>	2,3	10,6	1151	30,6	Blood.-5	2	2,3	1,5	1,5	0,6	2,27
<i>min</i>	1	2	200	2,0	Yes-4	0	0	0	0	0	0
<i>max</i>	6	31	3128	68,1	No-2	3	3	3	3	3	3

Before FMT








































№	FN	IAC	GVHD GI	Skin GVHD	Liver GVHD	General GVHD	Sepsis	antibiotics	antibiotics after FMT	Dynamics	Cause of severity of the condition
1	Н.В.	15	4	2	1	4	no	Stop	no	neg.	colitis
2	П.А.	9	3	2	4	4	no	Stop	Yes	neg.	Colitis, Liver GVHD
3	М.Д.										
4	С.А.										
5	А.Н.	13	4	3	4	4	sepsis	Stop	Yes	neg.	Colitis, encephalopathy
6	В.А.	16	4	2	3	4	sepsis	Stop	Yes	neg.	Colitis, cystitis
7	Т.Д.										
8	Ш.А.	11	3	2	1	3	no	Stop	Yes	neg.	Colitis
9	К.К.	16	4	0	4	4	septic shock	no	Yes	neg.	Colitis, hemorrhage, ventilation
10	Ф.И.	6	2	2	1	3	no	Stop	Yes	neg.	Colitis, pneumonia
11	Ф.А.	5	1				no	Stop	Yes	no	Hydrotorax
12	М.А.	16	4	2	4	4	sepsis	no	Yes	neg.	Colitis, Liver GVHD
13	П.М.	16	4	2	4	4	sepsis	no	Yes	neg.	Colitis, hemorrhage, ventilation
14	Л.А.	11	3	0	1	3	no	no	Yes	Neg.	Colitis

	IAC	GVHD GI	Skin GVHD	Liver GVHD	General GVHD	Sepsis	antibiotics	antibiotics after FMT	Dynamics
<i>min</i>	5	2	0	1	3	sepsis-5	a/b-4	a/b after FMT-10	Neg.-11
<i>med</i>	12,2	3,5	1,7	2,6	3,7	No sepsis-6	No a/b-7	No a/b-1	No dynamics-1
<i>max</i>	16	4	3	4	4				

After FMT

№	FN	<i>C.Difficile</i> tox. before	<i>C.Difficile</i> tox. D+30	D + decrease in symptoms 2 times		D + complete cessation of symptoms (3 d)					D+ (3 d)
				Frequency of stool	Stool volume	Blood in the stool	Mucus in the stool	Nausea	Vomiting	Pain	Appetite +1
1	H.B.	<u>B+</u>	<u>B-</u>	7	8	20	22	2	3	8	3
2	П.А.	B+	B+	12	11	12	18	4	6	5	6
3	М.Д.										
4	С.А.										
5	А.Н.	<u>B+</u>	<u>B-</u>	14	19	22	23	5	17	28	14
6	В.А.	B+	B+	28	30	10	97	62	55		59
7	Т.Д.										
8	Ш.А.	<u>B+</u>	<u>B-</u>	39	25	3	4	.-	.-	12	16
9	К.К.	B+	B+	36	10	27	39	31	31	31	36
10	Ф.И.	B-	B-	1	1	.-	.-	.-	.-	.-	.-
11	Ф.А.	B-	B-	.-	.-	.-	.-	.-	.-	.-	.-
12	М.А.	<u>B+</u>	<u>B-</u>	22	23	2	5	14	23	7	3
13	П.М.	B+	B+	.-	.-	.-	.-	.-	.-	.-	.-
14	Л.А.	B-	B-	7	7	7	.-	10	.-	.-	.-

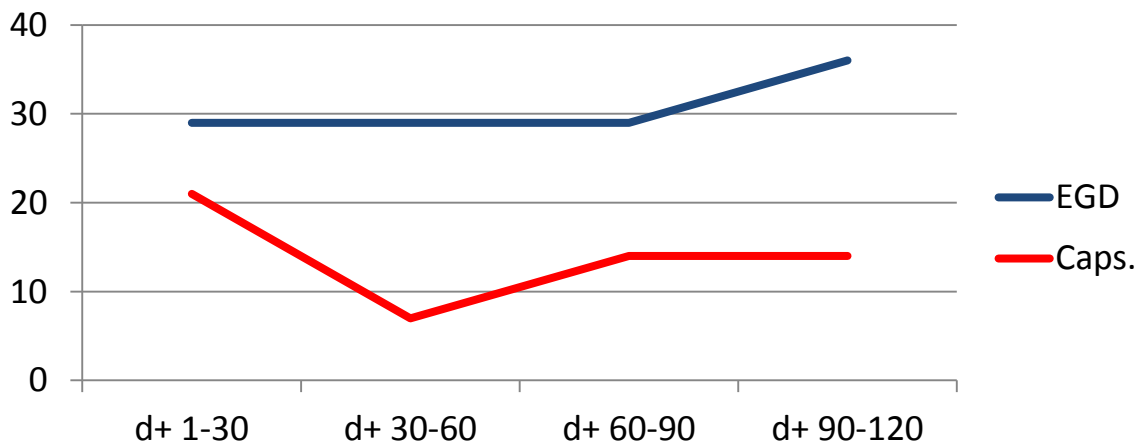
<i>B+/B - 4</i>		D + decrease in symptoms 2 times		D + complete cessation of symptoms (3 d)					D+ (3 d)
		Frequency of stool	Stool volume	Blood in the stool	Mucus in the stool	Nausea	Vomiting	Pain	Appetite +1
	<i>med</i>	18	14	13	30	18	22	15	19
	<i>min</i>	1	1	2	1	2	3	5	3
	<i>max</i>	39	11	11	97	62	55	31	59

№	Manag	EGD	pre	d+ 1-30	d+ 30-60	d+ 60-90	d+ 90-120	D+FMT	D+HSCT	Exodus			
1	H.B.	EGD						1137	2016	alive	Ch. Skin GVHD		
2	П.А.	EGD						1003	1227	alive	Ch. Liver GVHD		
3	М.Д.	EGD					125	239	dead	relapse			
4	С.А.	EGD					464	613	dead	relapse			
5	А.Н.	EGD						830	902	alive			
6	В.А.	Caps.					669	743	alive	Ch. Skin GVHD			
7	Т.Д.	Caps.					468	566	dead	Sepsis			
8	Ш.А.	Caps.						296	401	жив	Second FMT		
9	К.К.	EGD						198	362	alive	Cachexia		
10	Ф.И.	Caps.						198	336	alive	O.B.P.L.		
11	Ф.А.	Caps.						198	882	alive			
12	М.А.	EGD						133	140	alive			
13	П.М.	EGD						27	82	dead	Sepsis		
14	Л.А.	Caps.						71	156	alive	Second FMT		
1	В.М.	EGD							10	107	dead	Sepsis	
2	З.О.	EGD							14	70	dead	Sepsis	
3	Ф.О.	EGD								60	76	alive	
			Full				no blood, no mucus, normal stool						
			Partial				there is no blood, there is slime, a volume decrease of 2 times						
			Minimum				blood veins, diarrhea						

Results

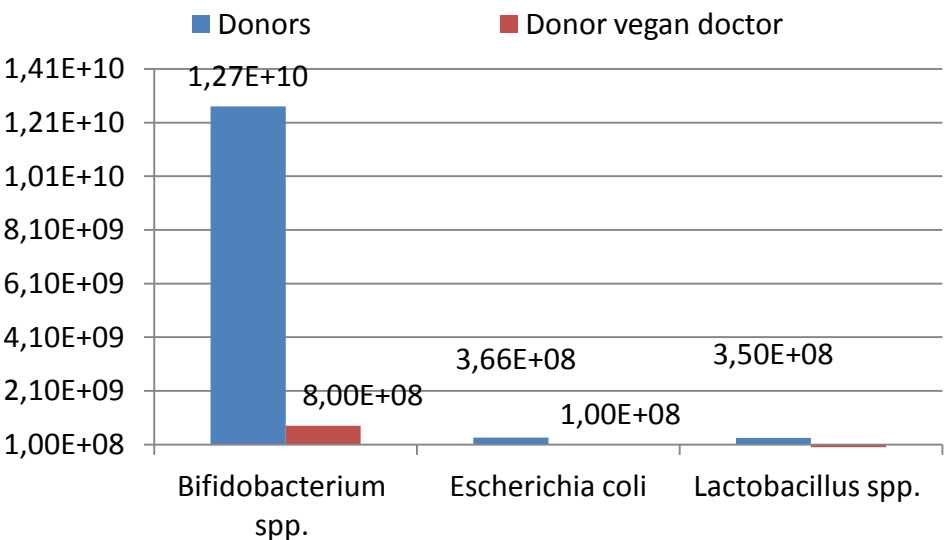
		d+ 1-30	d+ 30-60	d+ 60-90	d+ 90-120
Complete response%	14 patients	50	36	43	50
Complete response %	11 patients	64	45	55	64

			d+ 1-30	d+ 30-60	d+ 60-90	d+ 90-120
Complete response%	14 пац.	EGD	29	29	29	36
Complete response%	14 пац.	Caps.	21	7	14	14

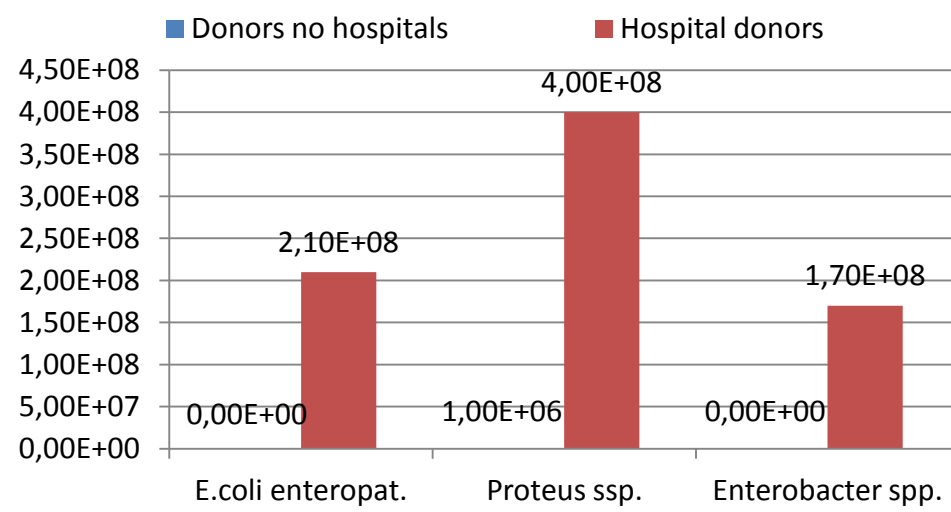


PCR-16		DONORS FT					
No	Donor	FMT	Sex	Relation	Age	Life - hospital	Note
1	1	unrelated donor	f	no	33	no	
2		unrelated donor	f	no	33	no	200 d
3		unrelated donor	f	no	33	no	200 d
4		unrelated donor	f	no	33	no	200 d
5	2	unrelated donor	m	no	16	no	
6	3	unrelated donor	m	no	36	Yes	vegan doctor
7	4	related donor	f	mother	33	Yes	
8	5	related donor	m	father	40	Yes	
9	6	related donor	m	brother	33	Yes	
10	7	related donor	m	father	34	Yes	

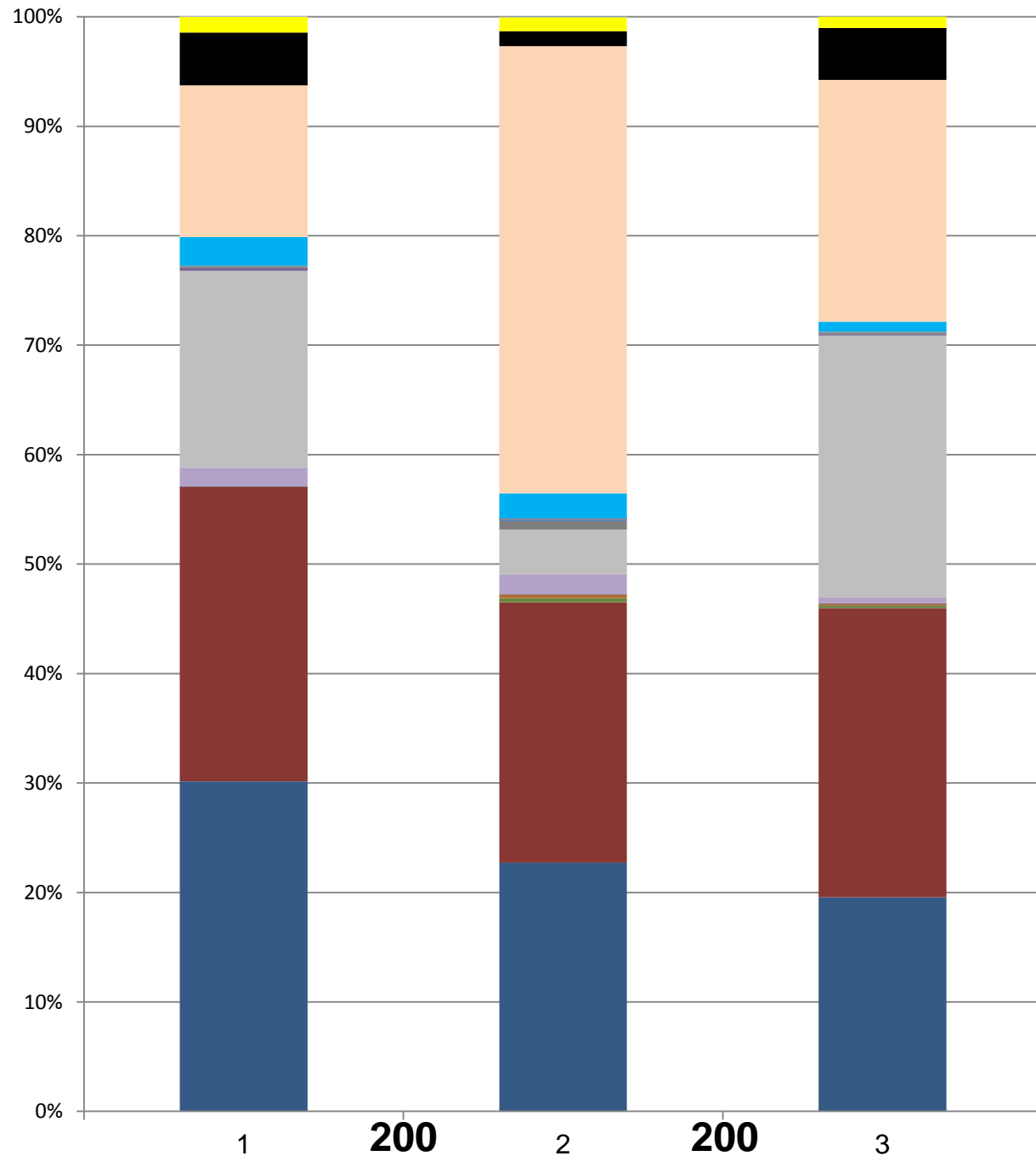
DONOR IS NOT VEGAN



DONOR IS NOT INSIDE THE HOSPITAL



16S rRNA Family



- Lachnospiraceae
- Ruminococcaceae
- Bacteroidaceae
- Porphyromonadaceae
- Veillonellaceae
- Prevotellaceae
- Acidaminococcaceae
- Erysipelotrichaceae
- Rikenellaceae
- Enterococcaceae
- Streptococcaceae



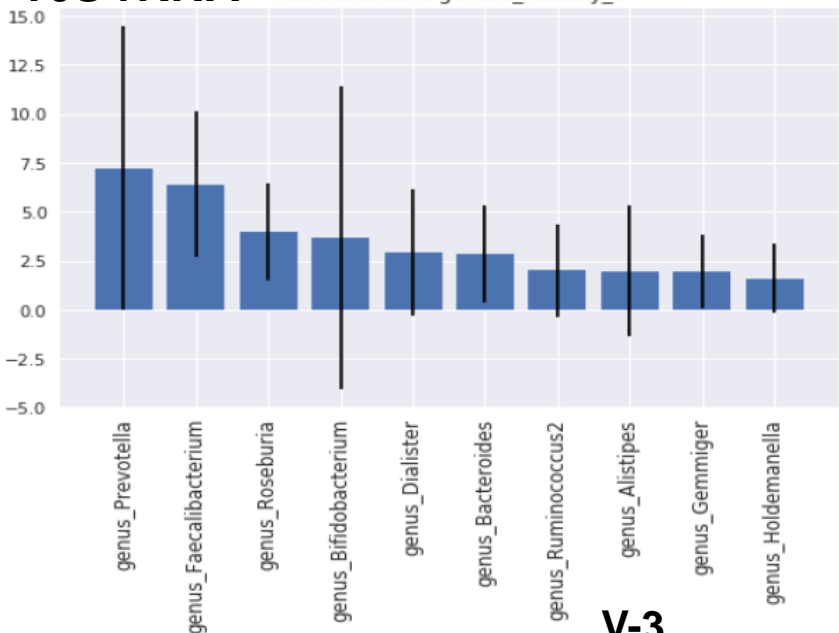
d

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 Россия

Сидоренко С.В., Гостев В.А., Лобзин Ю.В. ФГБУ ДНКЦИБ ФМБА России

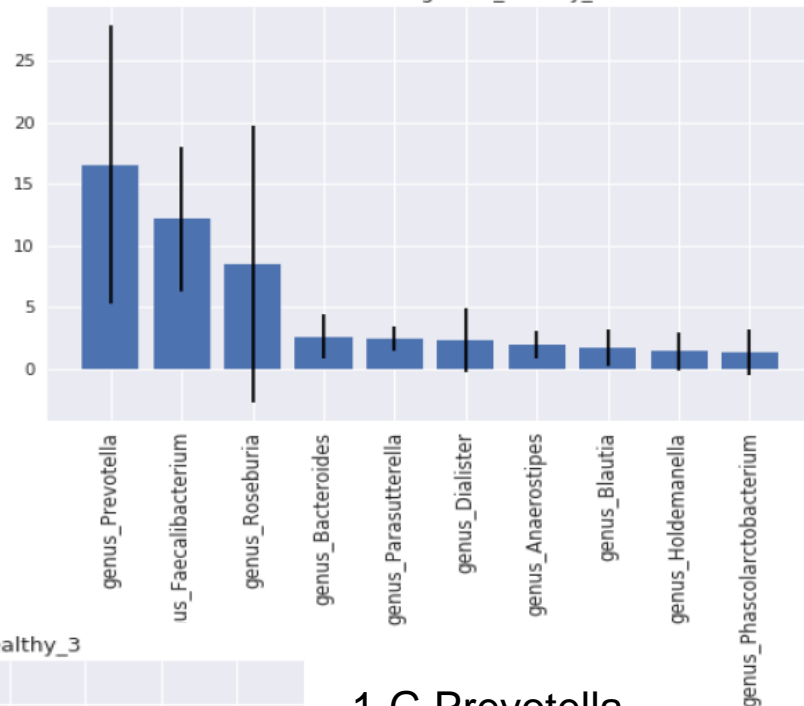
16S rRNA

most abundant genera_healthy_1



V-1

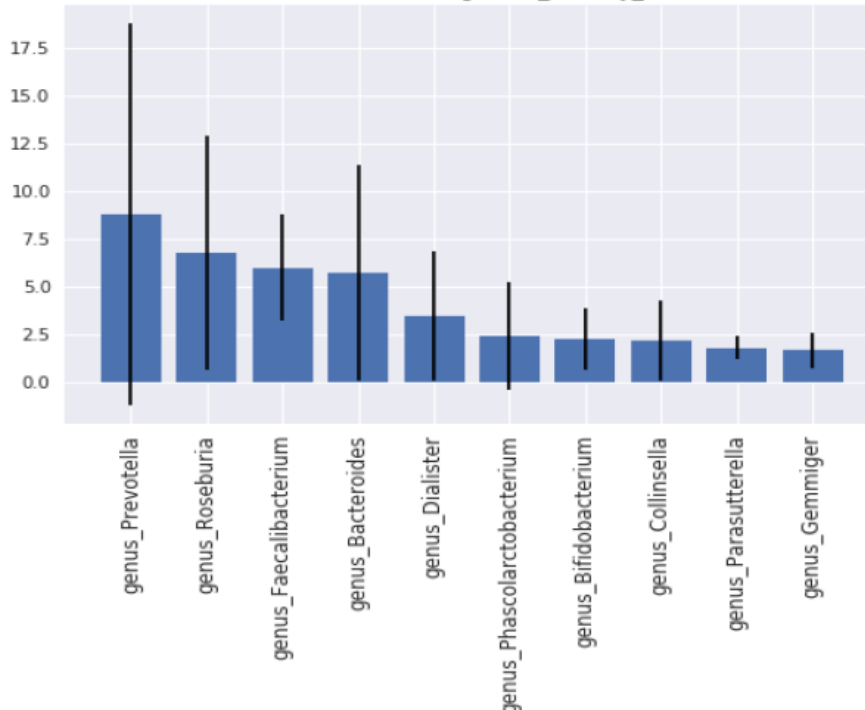
most abundant genera_healthy_2



V-2

V-3

most abundant genera_healthy_3



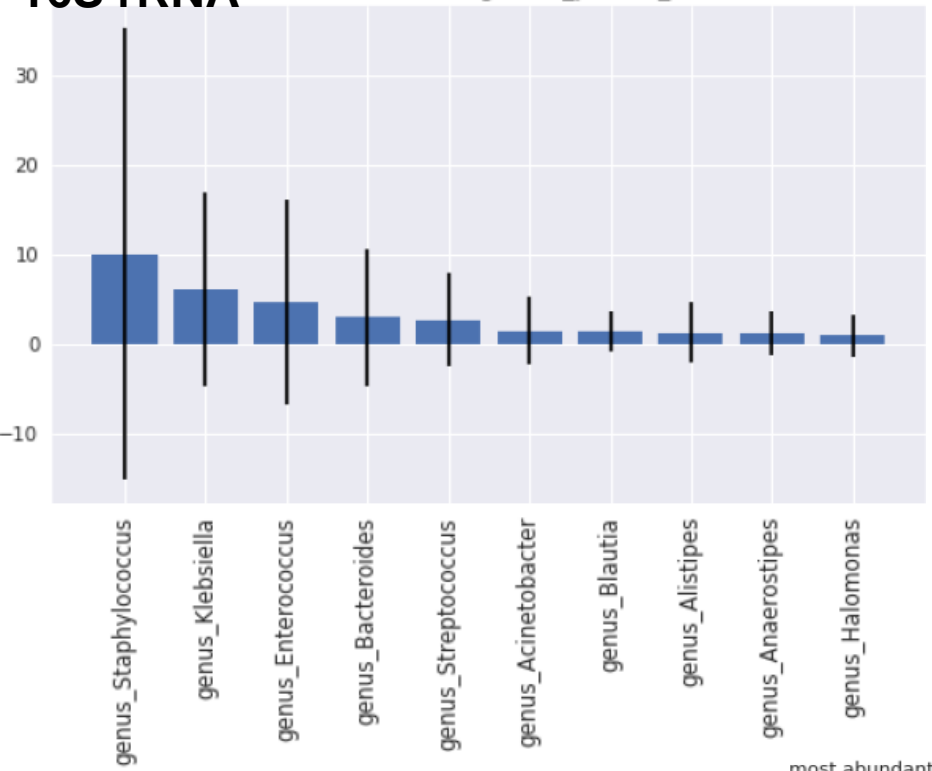
- 1-G.Prevotella
- 2-G.Faecalibacterium
- 3-G.Roseburia
- 4-G.Bifidobacterium

- 1-G.Prevotella
- 2-G.Faecalibacterium
- 3-G.Roseburia
- 4-G.Bacteroides

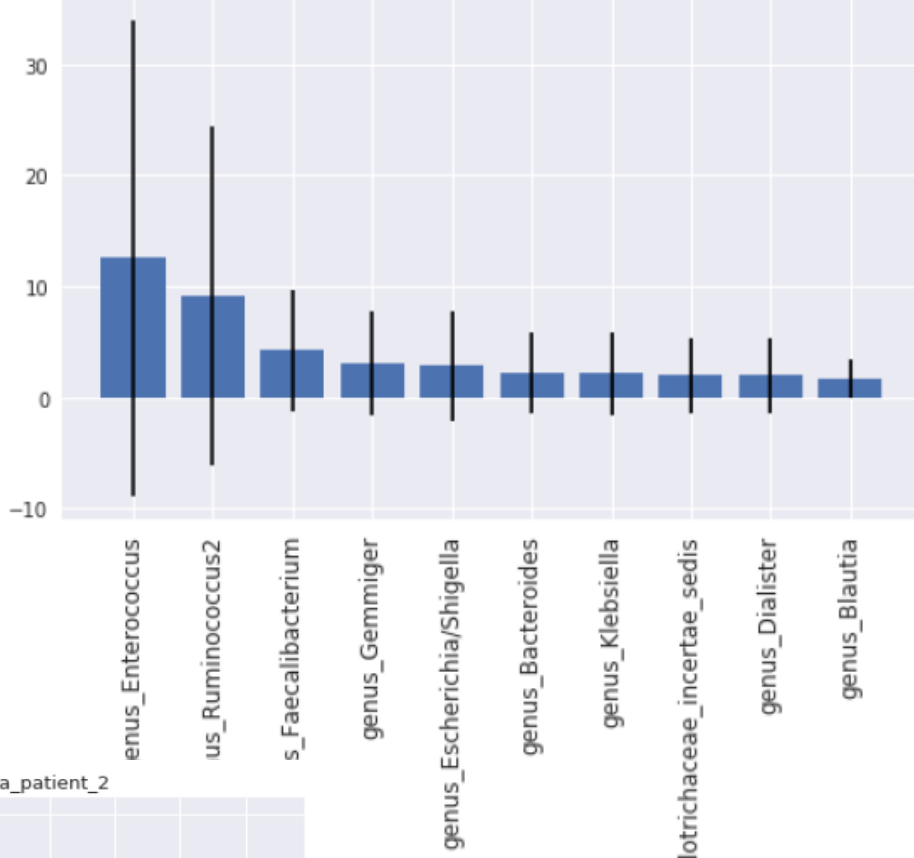
- 1-G.Prevotella
- 2-G.Roseburia
- 3-G.Faecalibacterium
- 4-G.Bacteroides

16S rRNA

most abundant genera_patient_1

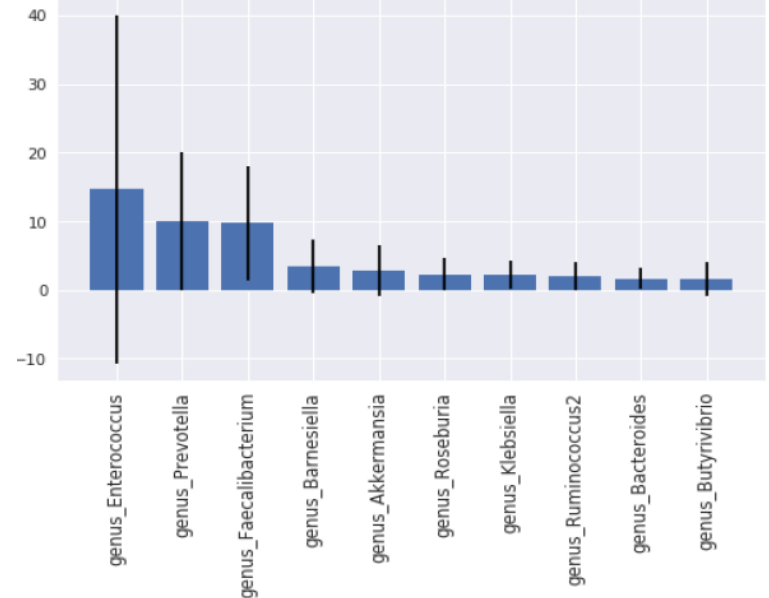


most abundant genera_patient_3



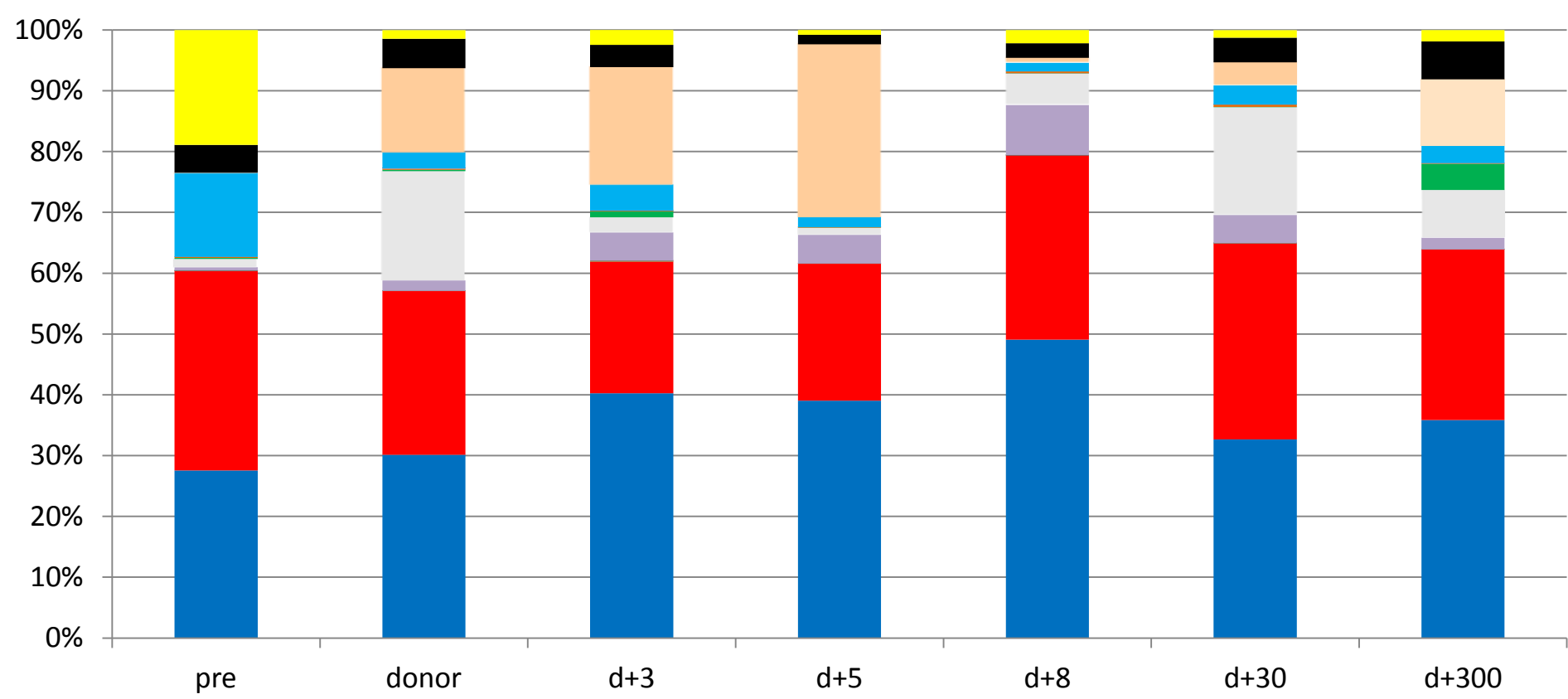
- 1-G.Staphylococcus
- 2-G.Klebsiella
- 3-G.Enterococcus
- 4-G. Bacteroides

most abundant genera_patient_2



- 1-G.Enterococcus
- 2-G.Ruminococcus
- 3-G. Faecalibacterium

- 1-G.Prevotella
- 2-G.Enterococcus
- 3-G.Faecalibacterium

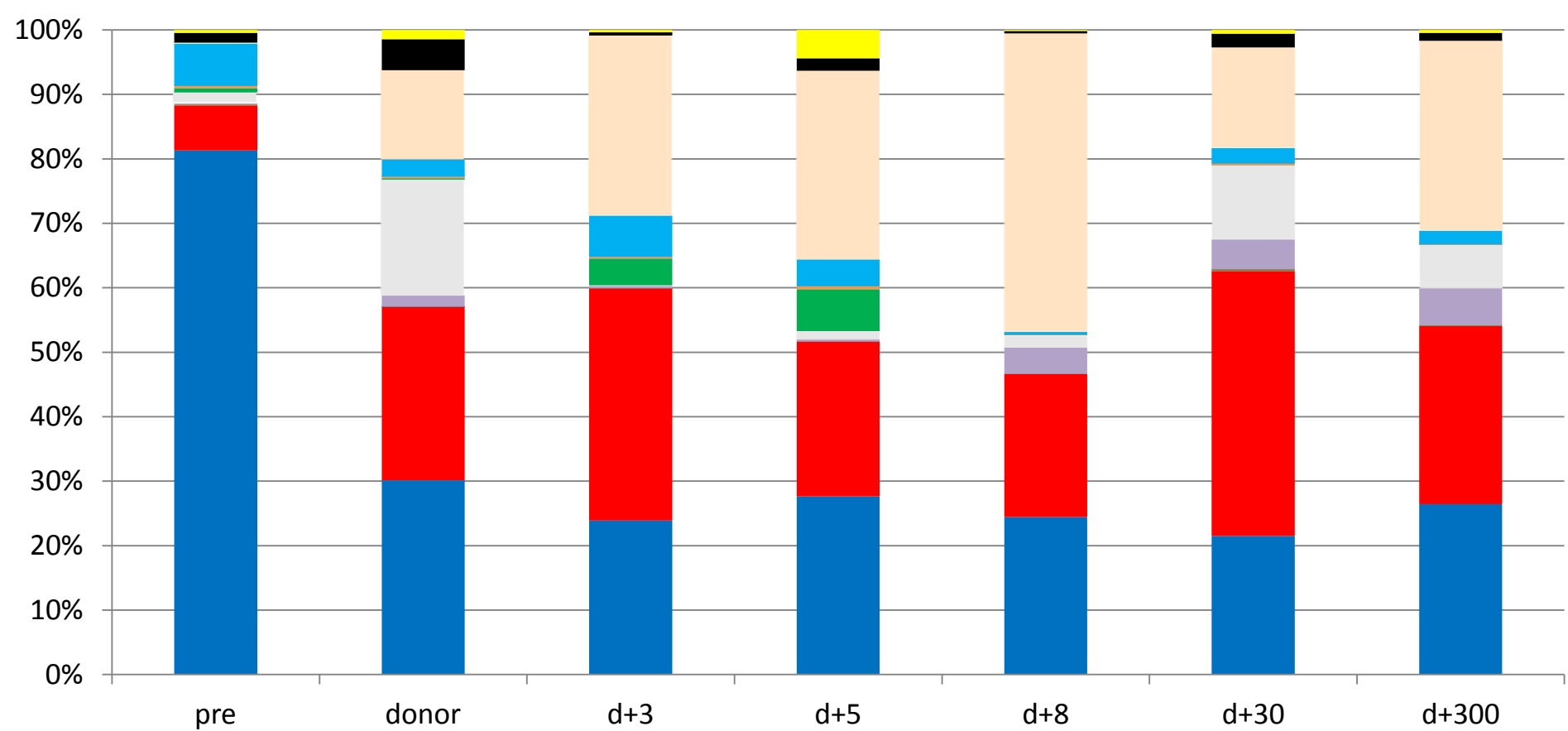


V-1 **Change of enterotypes?**

Family 16S rRNA

- Lachnospiraceae
- Ruminococcaceae
- Bacteroidaceae
- Porphyromonadaceae
- Veillonellaceae
- Prevotellaceae
- Acidaminococcaceae
- Erysipelotrichaceae
- Rikenellaceae
- Streptococcaceae
- Enterococcaceae



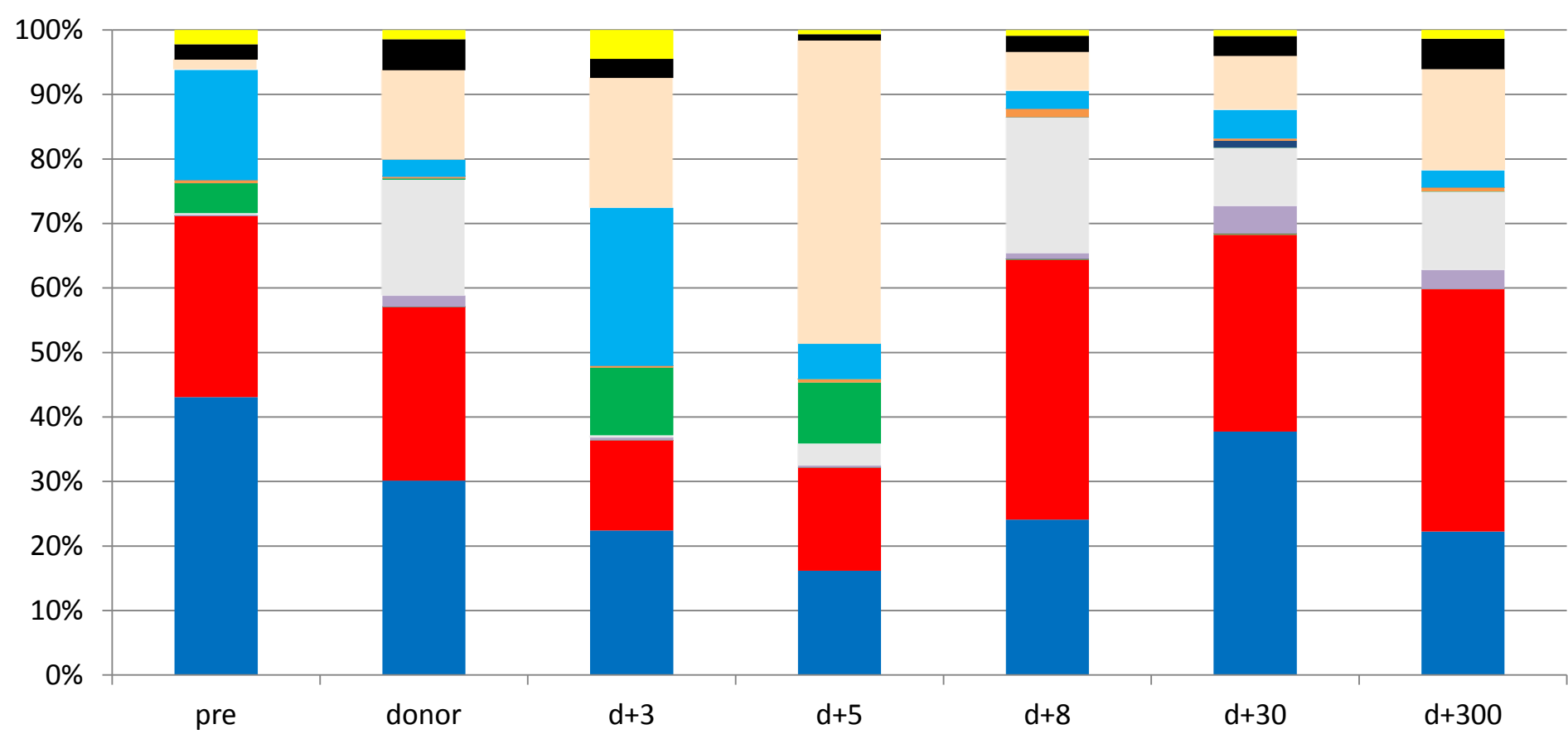


Lachnospiraceae
 Ruminococcaceae
 Bacteroidaceae
 Porphyromonadaceae
 Veillonellaceae
 Prevotellaceae
 Acidaminococcaceae
 Erysipelotrichaceae
 Rikenellaceae
 Streptococcaceae
 Enterococcaceae



V-2 **Change of enterotypes?**

Family 16S rRNA



V-3

Change of enterotypes?

Family 16S rRNA

- Lachnospiraceae
- Ruminococcaceae
- Bacteroidaceae
- Porphyromonadaceae
- Veillonellaceae
- Prevotellaceae
- Acidaminococcaceae
- Erysipelotrichaceae
- Rikenellaceae
- Streptococcaceae
- Enterococcaceae



Importance of changes in bacterial content of microbiota

In comparison with the moment to FMT

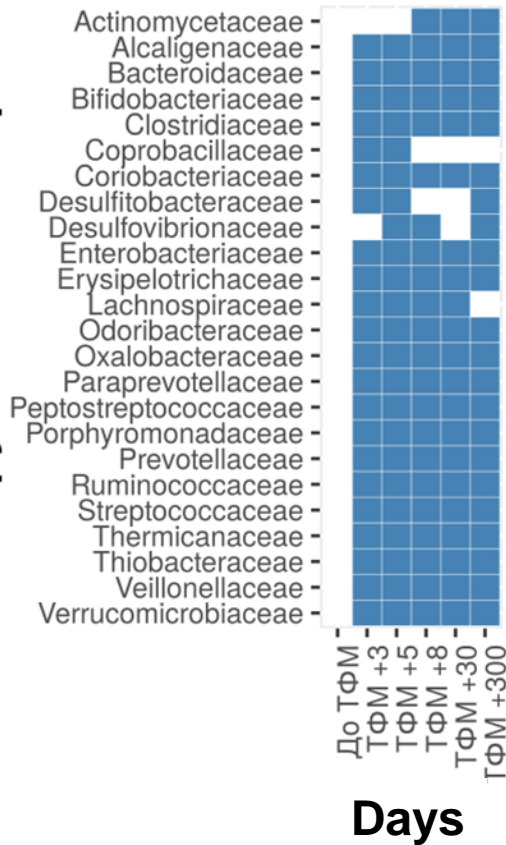
($p < 0.05$)

Volunteer №1

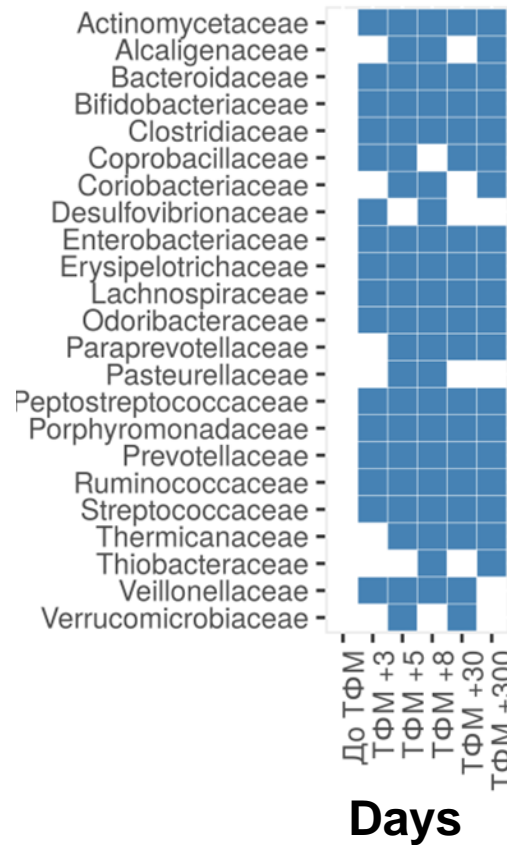
Volunteer №2

Volunteer №3

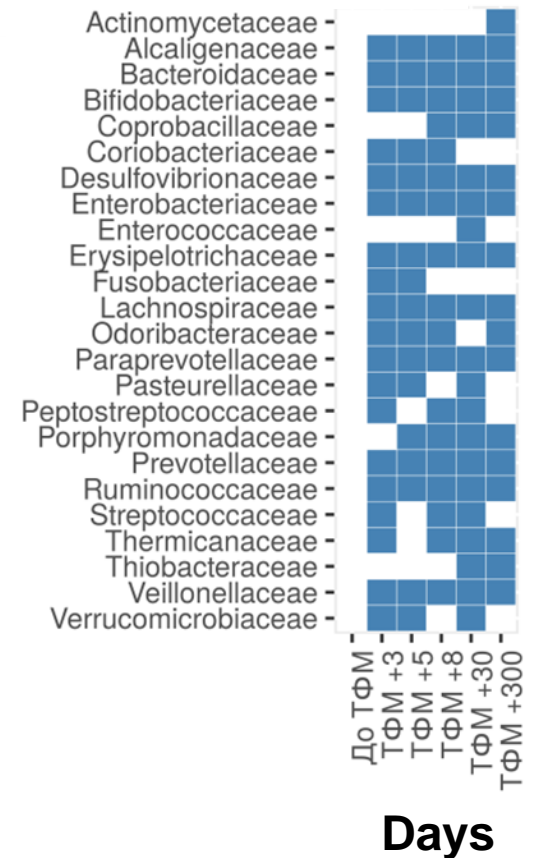
Discovered bacteria



Discovered bacteria



Discovered bacteria

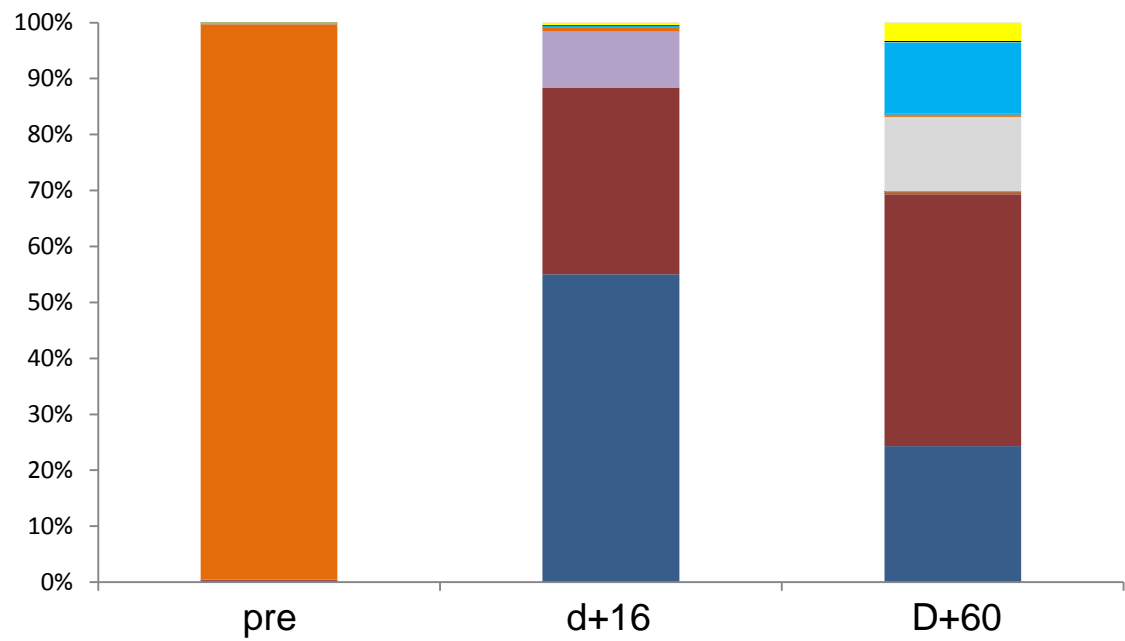
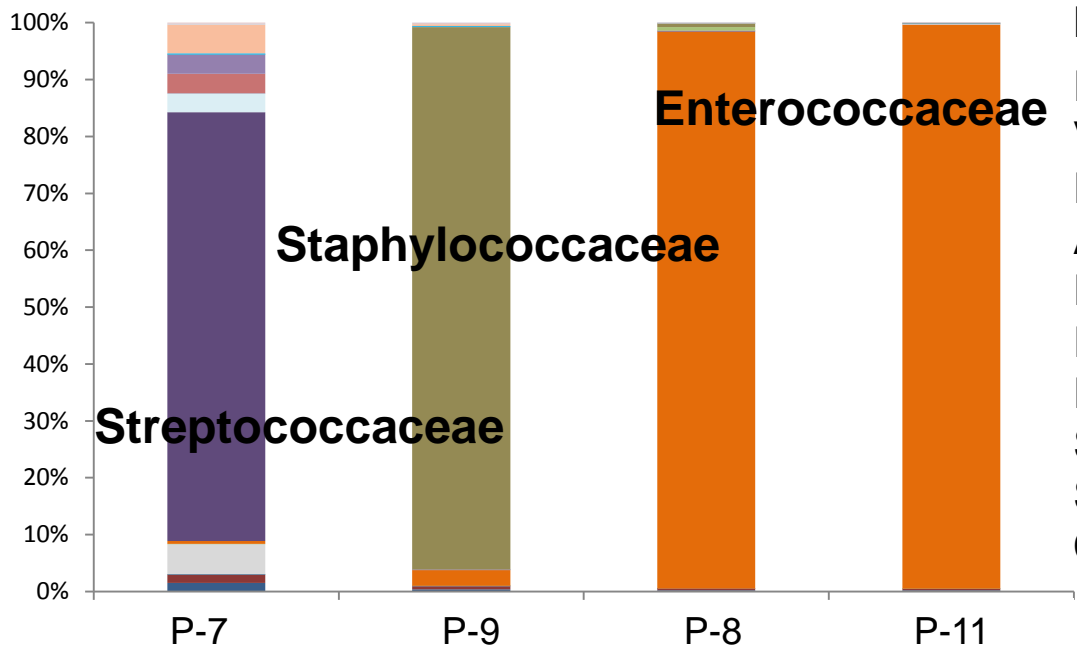


Volunteers (n=3, 100%) intestinal microbiota content significant changes D+300 after TFM

Actinomycetaceae
Alcaligenaceae
Bacteroidaceae
Bifidobacteriaceae
Enterobacteriaceae
Erysipelotrichaceae
Odoribacteraceae
Paraprevotellaceae
Porphyromonadaceae
Prevotellaceae
Ruminococcaceae
Thermicanaceae
Thiobacteraceae

PATIENTS BEFORE FMT

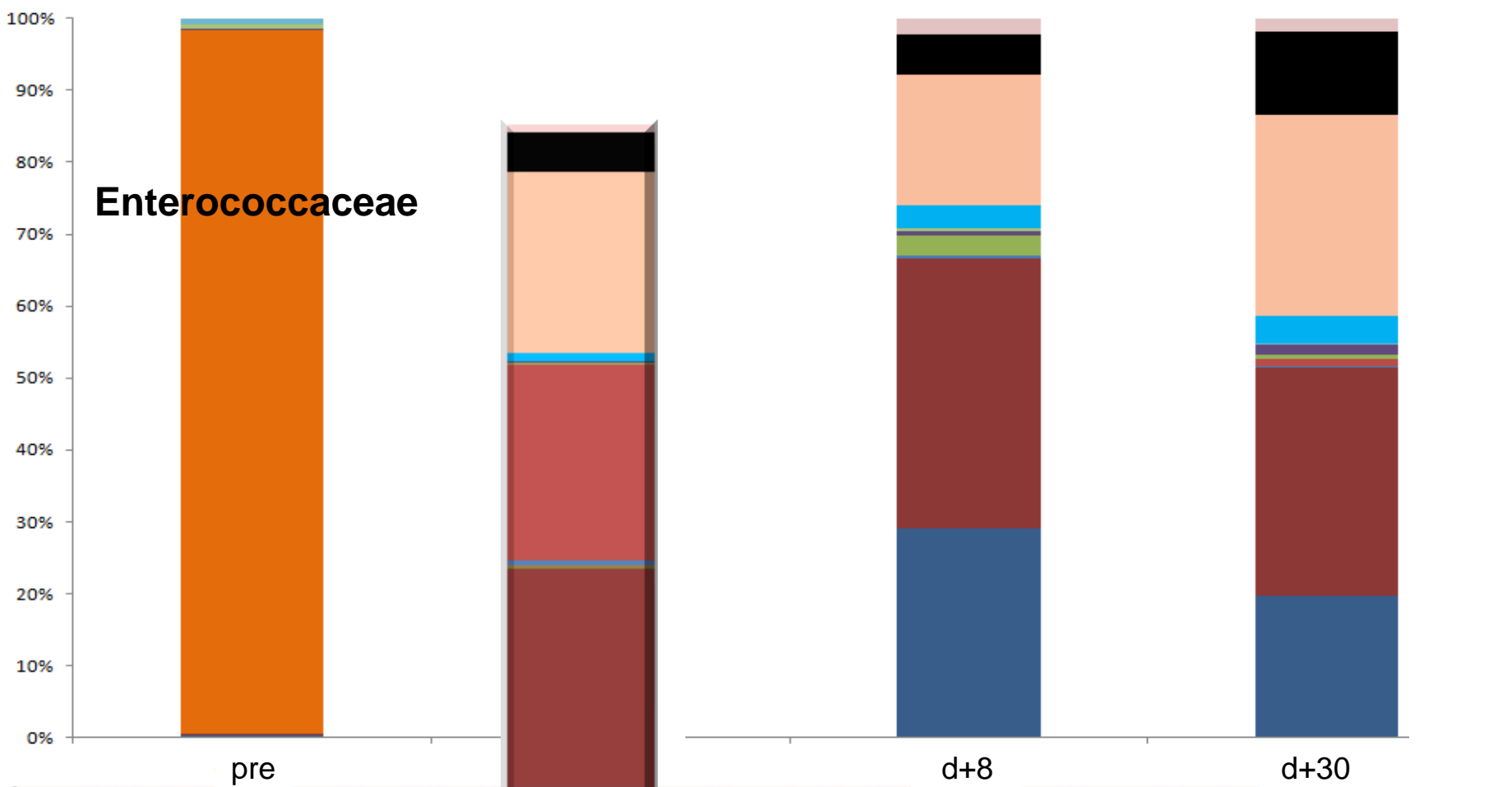
- Lachnospiraceae
- Ruminococcaceae
- Bacteroidaceae
- Porphyromonadaceae
- Veillonellaceae
- Prevotellaceae
- Acidaminococcaceae
- Erysipelotrichaceae
- Rikenellaceae
- Enterococcaceae
- Streptococcaceae
- Staphylococcaceae
- Carnobacteriaceae



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 ФГБУ ДНКЦИБ ФМБА России

P-Control
 16S rRNA

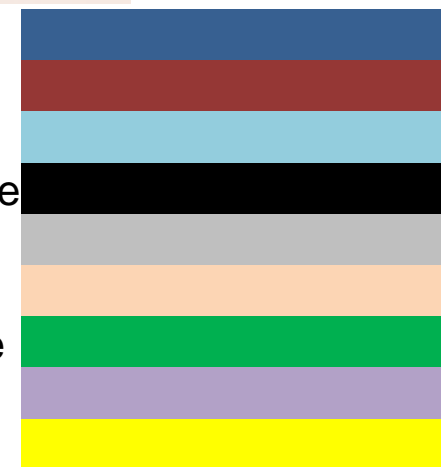


**BIOLOGICAL
DECONTAMINATION-?**

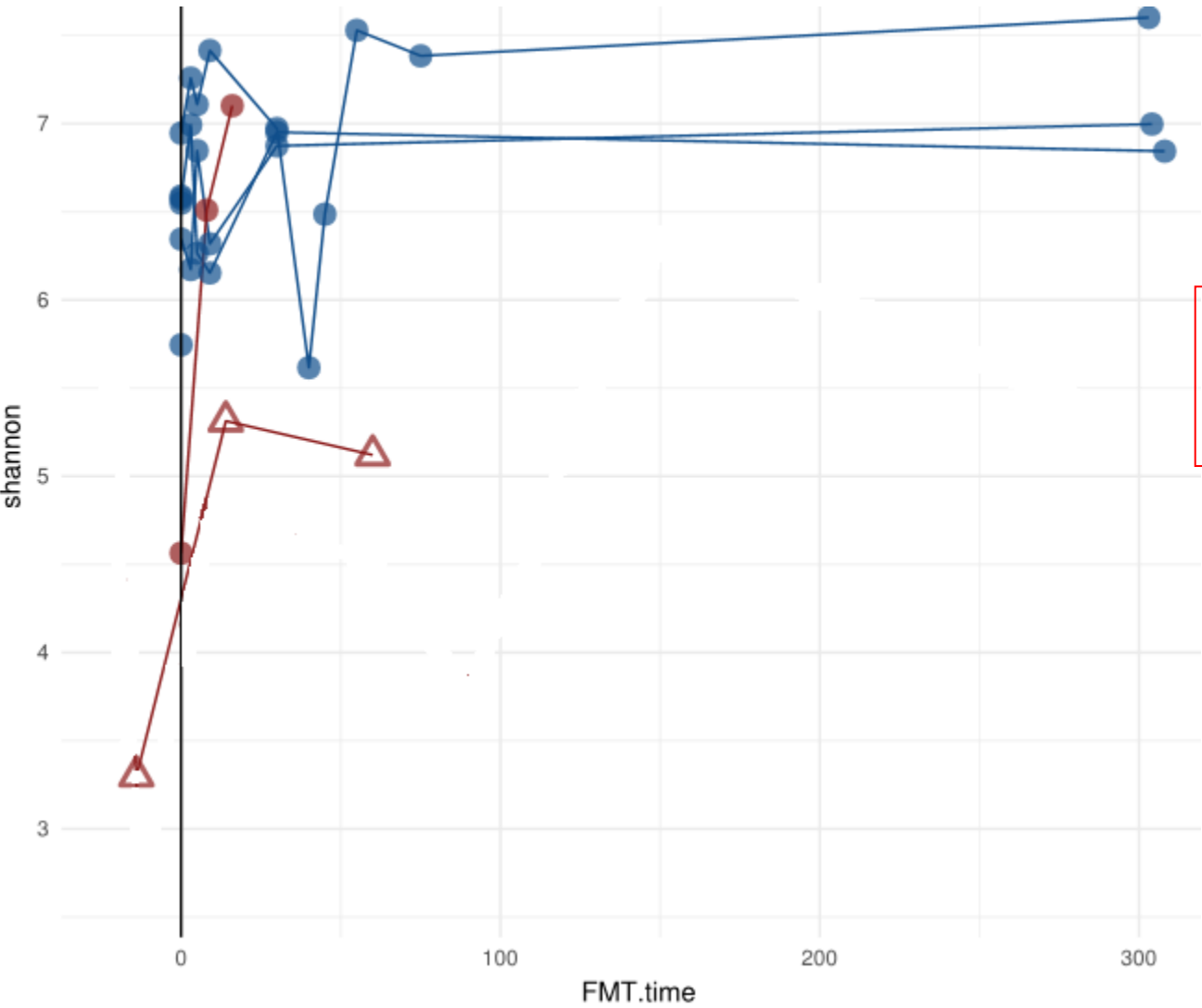
P-8 W.A.

Donor

Lachnospiraceae
Ruminococcaceae
Bacteroidaceae
Porphyromonadaceae
Veillonellaceae
Prevotellaceae
Acidaminococcaceae
Erysipelotrichaceae
Rikenellaceae



16S rRNA



Biota structure characterized by two parameters

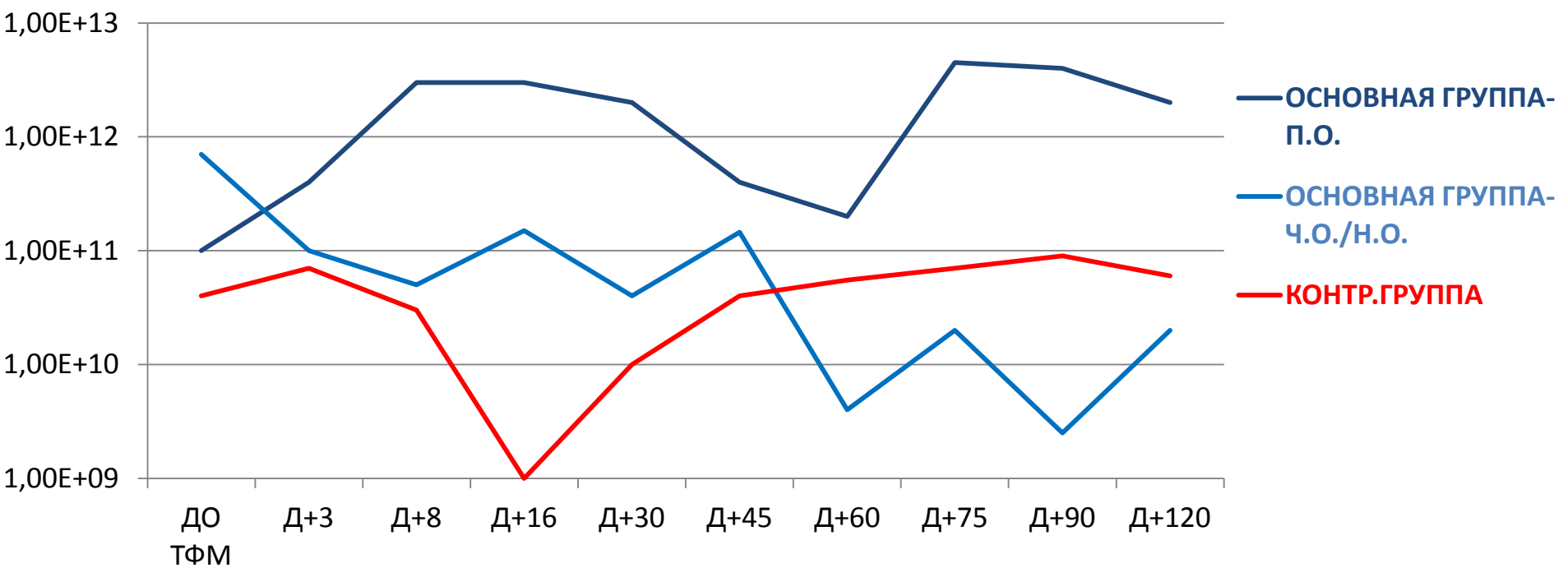
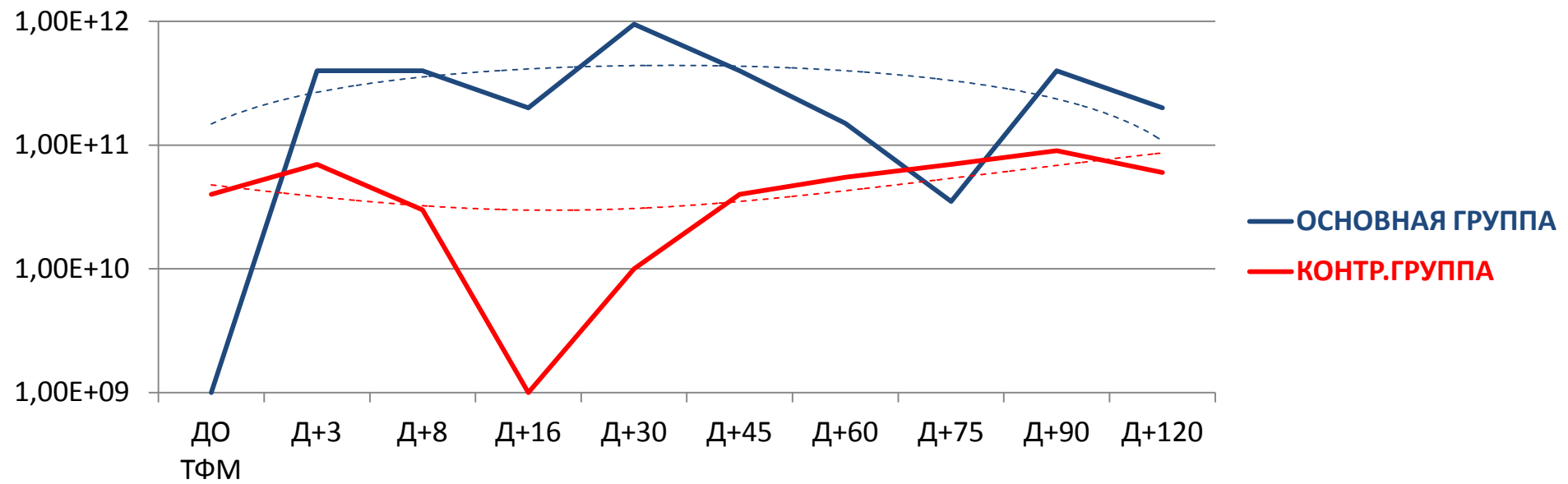
The larger the Shannon index, the more diverse the biota

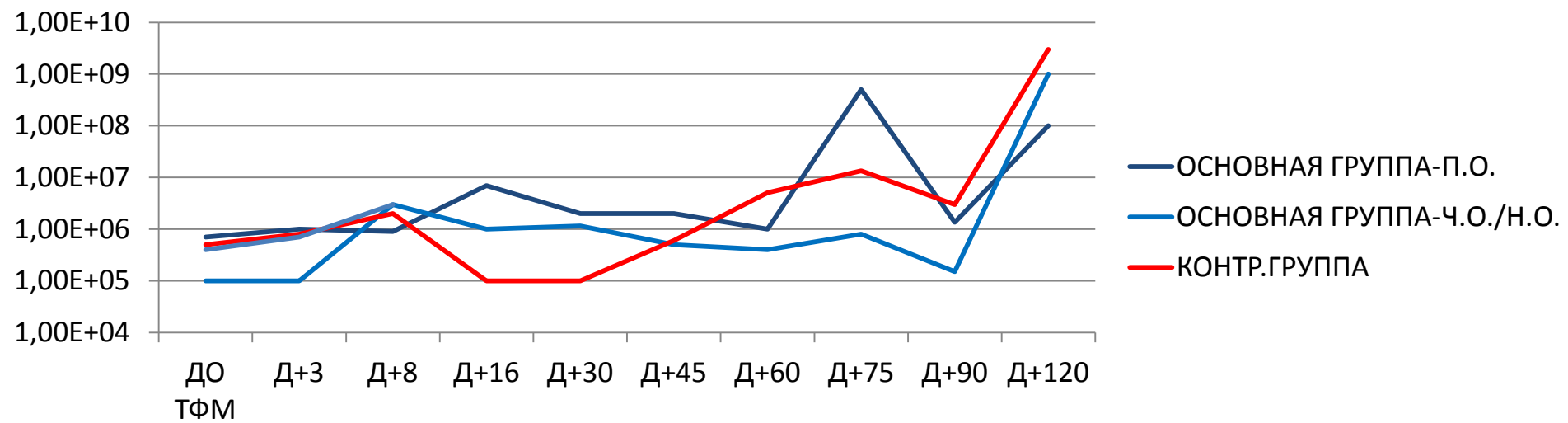
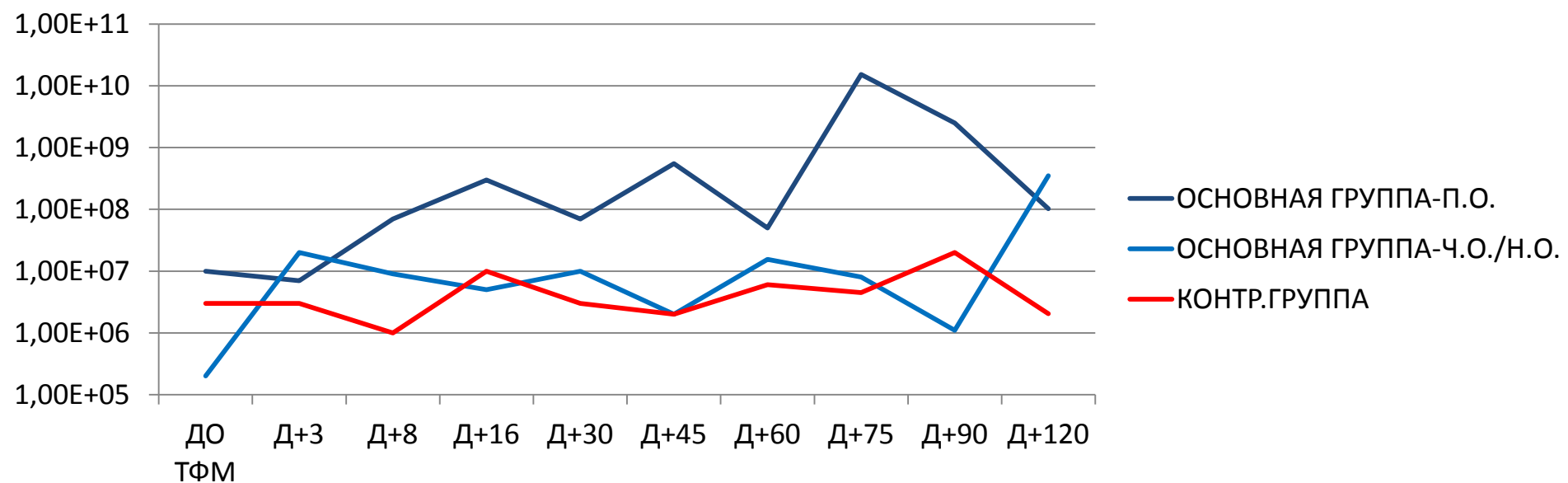
$$H = - \sum_{i=1}^n p_i \log_2 p_i$$

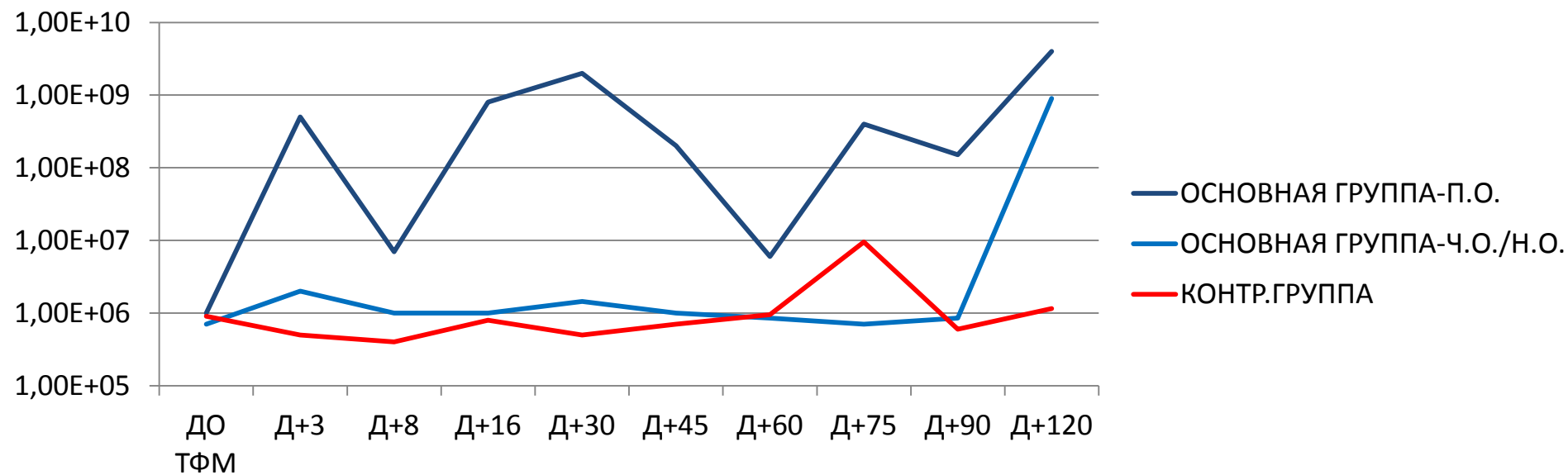
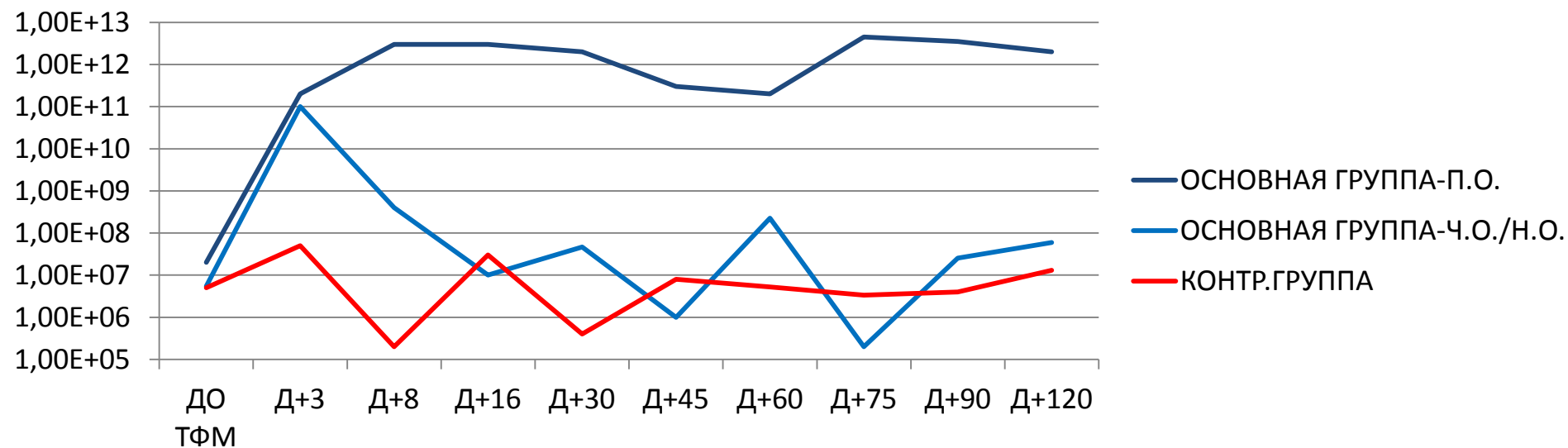
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ФНКЦ физико-химической медицины
ФМБА России, Москва, Россия

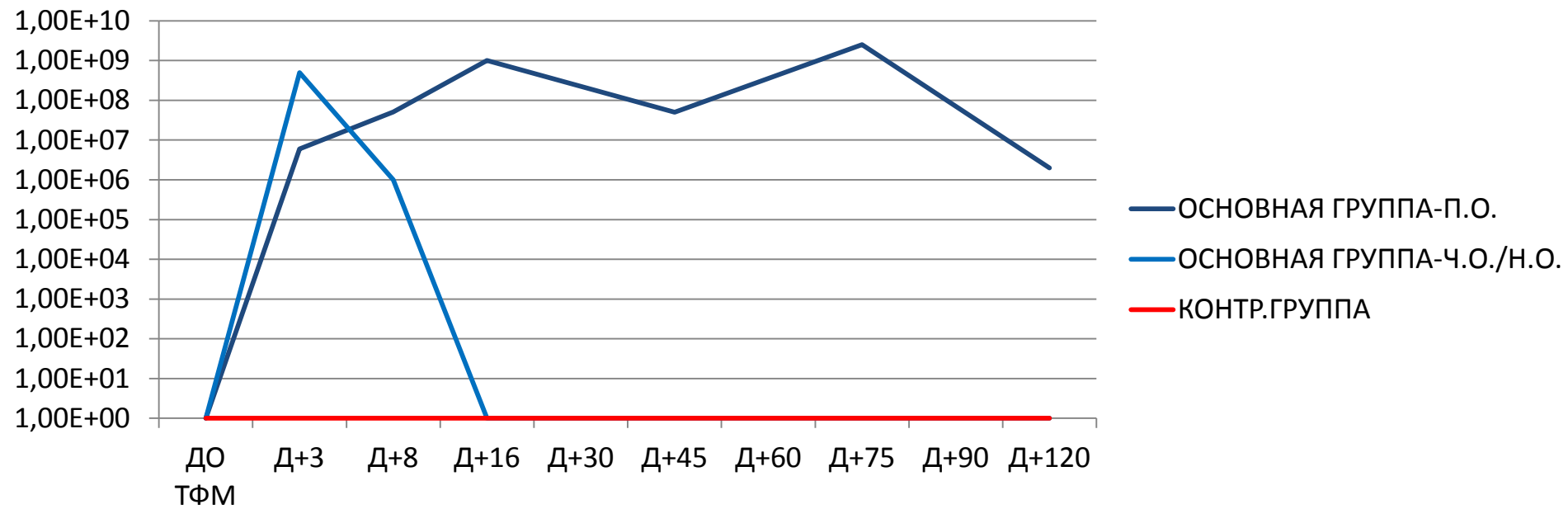
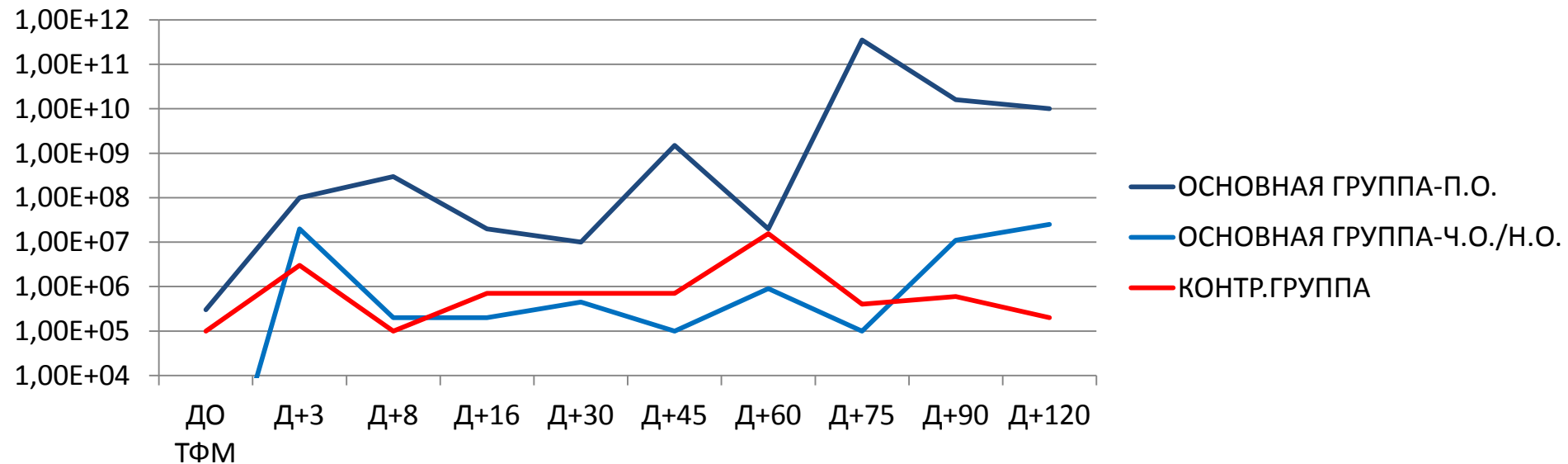
p_i - the proportion of the type of microorganism in the community (the fraction of a whole is unity)

n - the number of species of microorganisms (varies from 1 to n)



**Bifidobacterium spp.***Рост Д+16*

**Bacteroides fragilis group***Рост Д+3*

**Faecalibacterium prausnitzii***Рост Д+3*

**KLEBSIELLA
PNEUMONIAE**

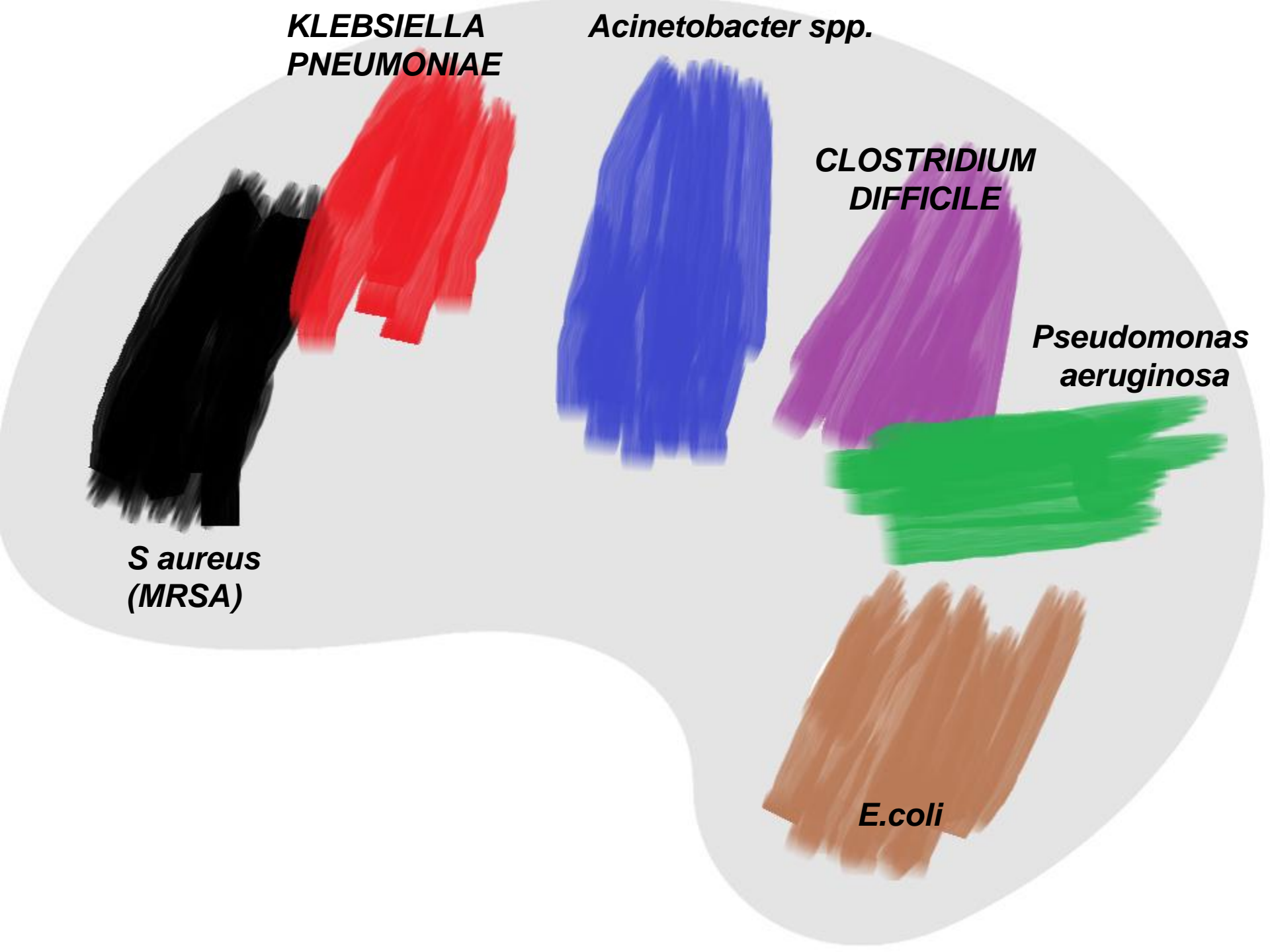
Acinetobacter spp.

**CLOSTRIDIUM
DIFFICILE**

**Pseudomonas
aeruginosa**

**S aureus
(MRSA)**

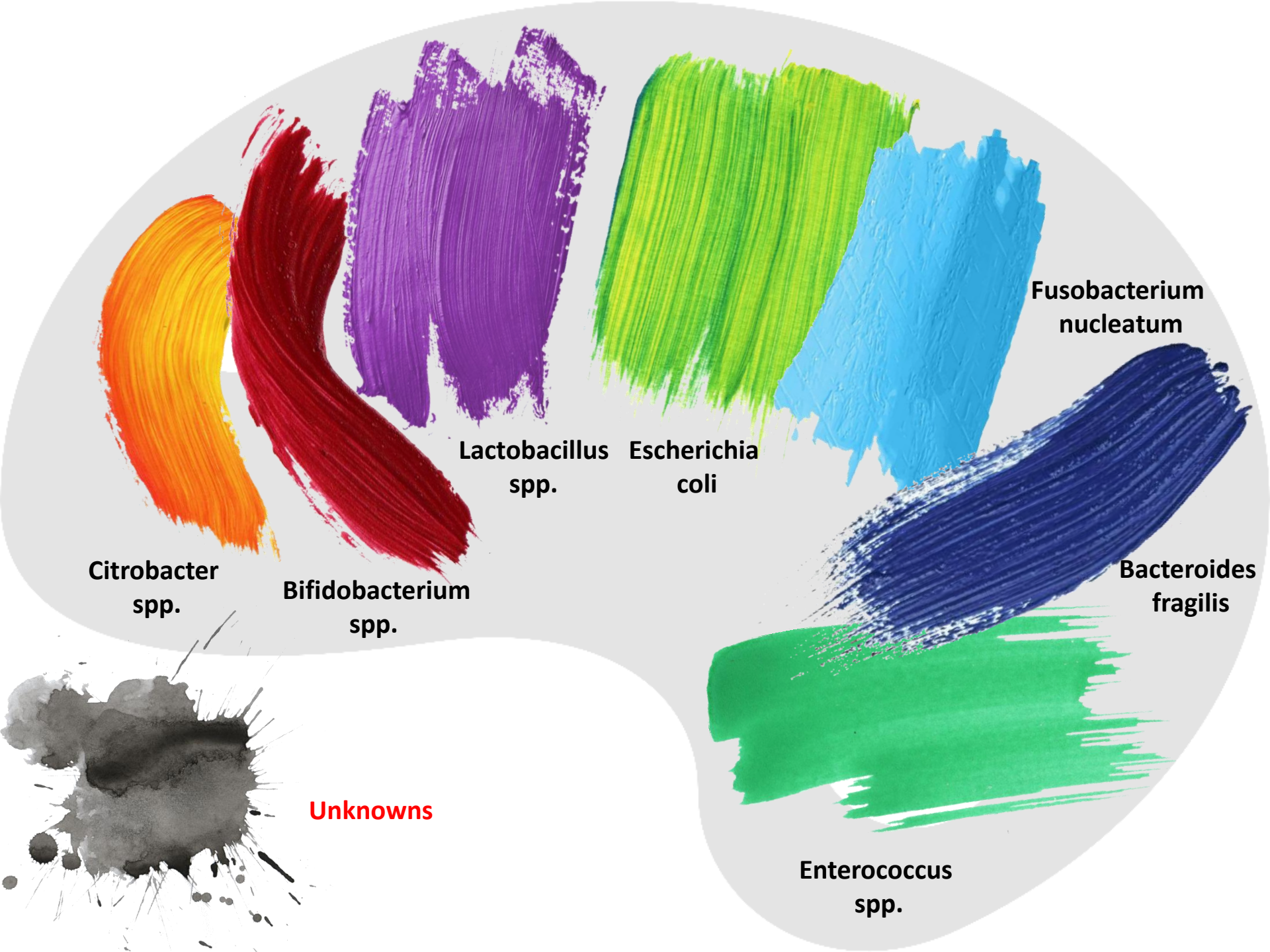
E.coli





«Микробный пейзаж»

Mouth bacteria: the good, the bad and the uglySteve Gschmeissner/Science Photo Library



**Citrobacter
spp.**

**Bifidobacterium
spp.**

**Lactobacillus
spp.**

**Escherichia
coli**

**Fusobacterium
nucleatum**

**Bacteroides
fragilis**

Unknowns

**Enterococcus
spp.**

	D+28 Mech.vent.(10 d)	D+0 BMT	Volunteers
Skin	<p>Citrobacter spp. Bifidobacterium spp. Enterococcus spp. Escherichia coli</p>	<p>Bacteroides fragilis Faecalibacterium prausnitzii Bifidobacterium spp.</p>	<p>Bifidobacterium spp. Escherichia coli Lactobacillus spp.</p>
Lavage	<p>Bacteroides fragilis Faecalibacterium prausnitzii Escherichia coli</p>	<p>Bacteroides fragilis Faecalibacterium prausnitzii</p>	<p>Нет данных</p>
Urine	<p>Bacteroides fragilis Bifidobacterium spp.</p>	<p>Bacteroides fragilis Bifidobacterium spp. Escherichia coli</p>	<p>Bifidobacterium spp. Lactobacillus spp.</p>
Saliva	<p>Enterococcus spp.</p>	<p>Bacteroides fragilis Bifidobacterium spp. Escherichia coli</p>	<p>Lactobacillus spp. Bifidobacterium spp. Bacteroides fragilis</p>
Duodenum	<p>Enterococcus spp.</p>	<p>Нет данных</p>	<p>Fusobacterium nucleatum Bifidobacterium spp. Bacteroides fragilis</p>
Feces	<p>Enterococcus spp.</p>	<p>Citrobacter spp.</p>	<p>Bacteroides fragilis Faecalibacterium prausnitzii</p>

Study group (n=16)

Placebo (n=7)

Full response

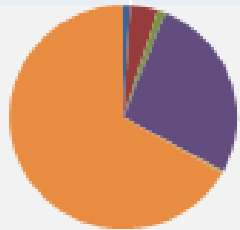
No response

Partial response

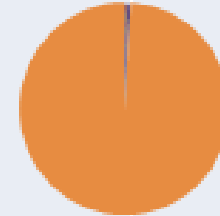
Full response

Before

Citrobacter spp.

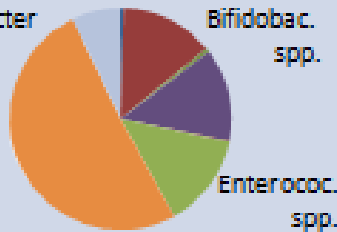


Citrobacter spp.

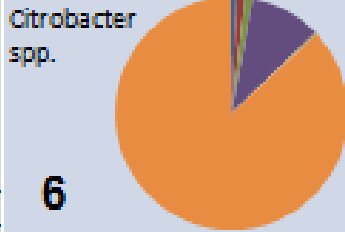


Before

10



6

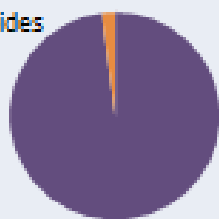


Citrobacter spp.

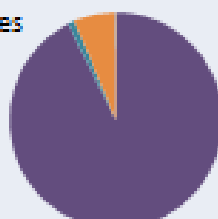


+3

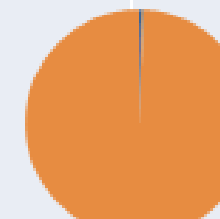
Bacteroides fragilis



Bacteroides fragilis



Citrobacter spp.

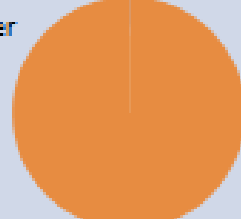


+8

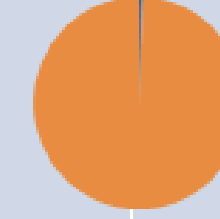
Bacteroides fragilis



Citrobacter spp.



Citrobacter spp.

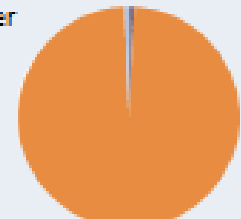


+16

Bacteroides fragilis



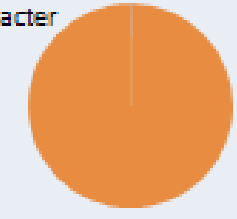
Citrobacter spp.



Citrobacter spp.

1

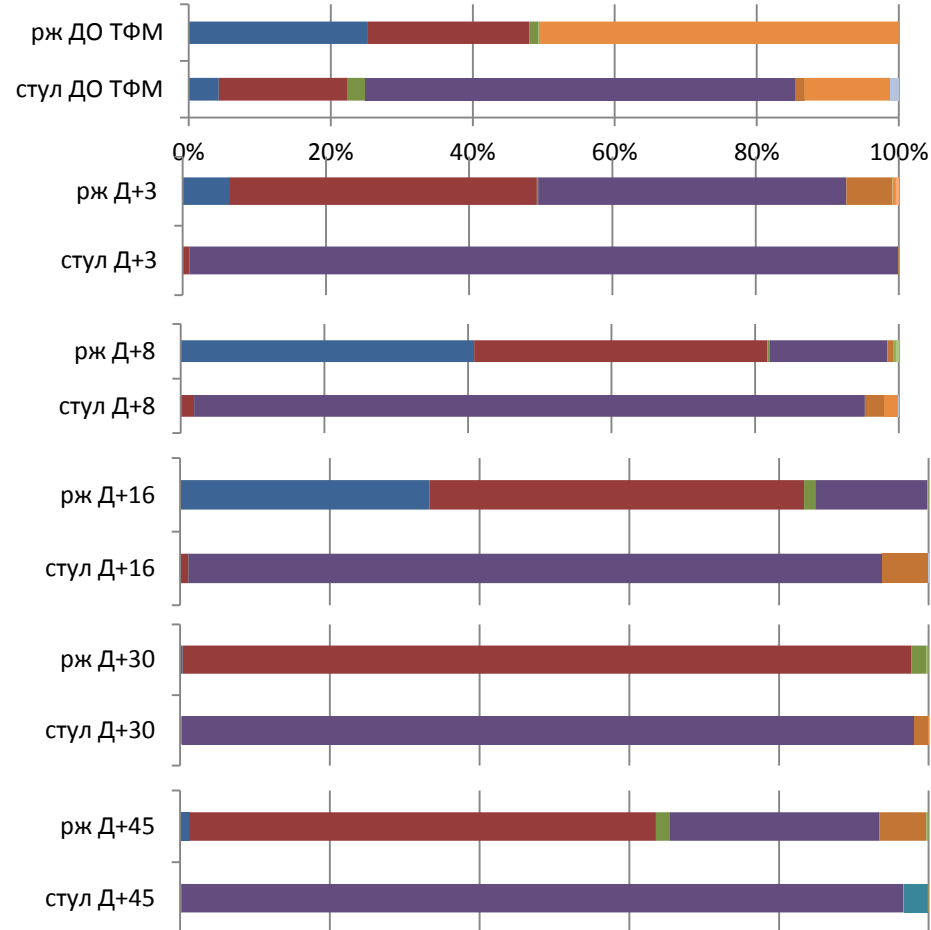
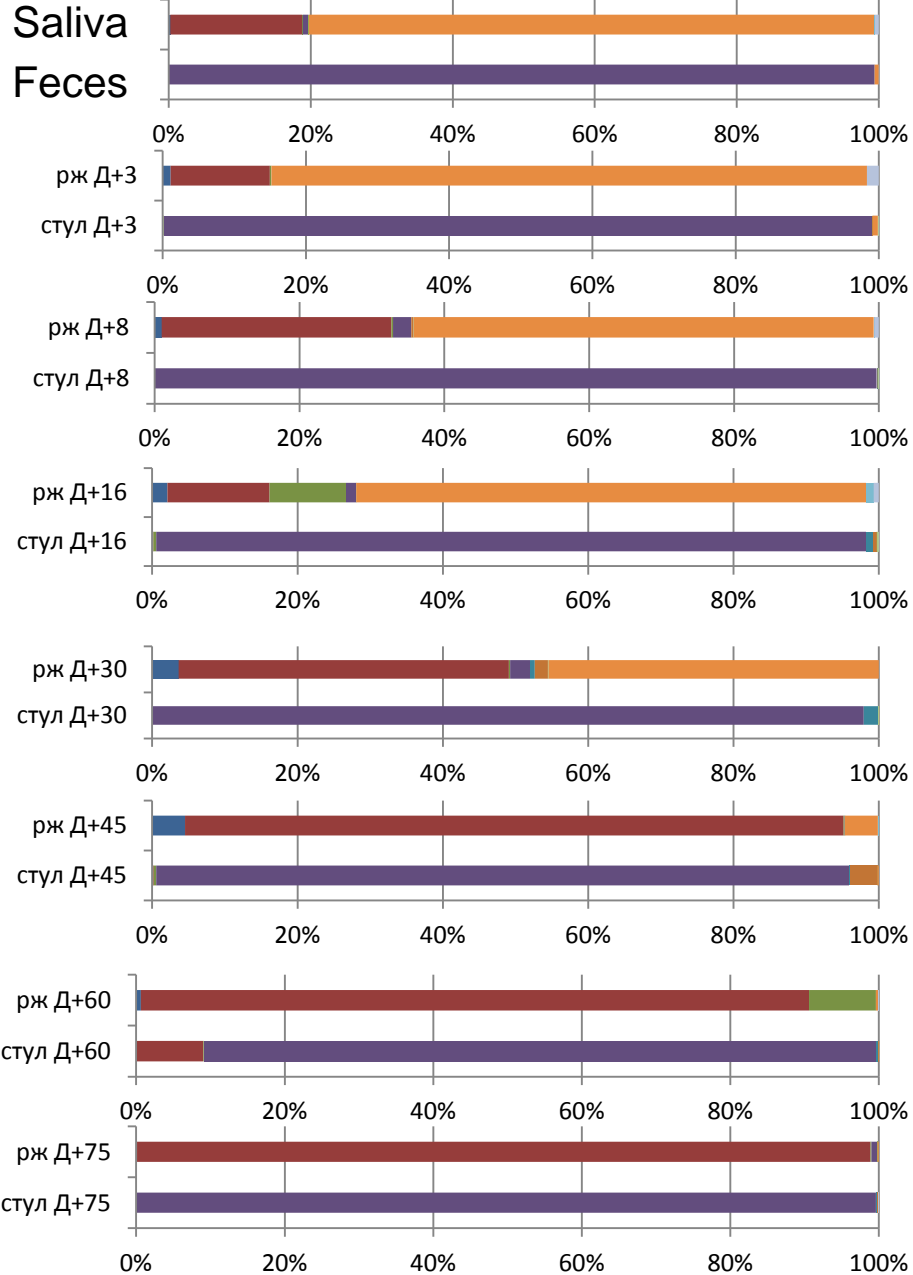
Citrobacter spp.



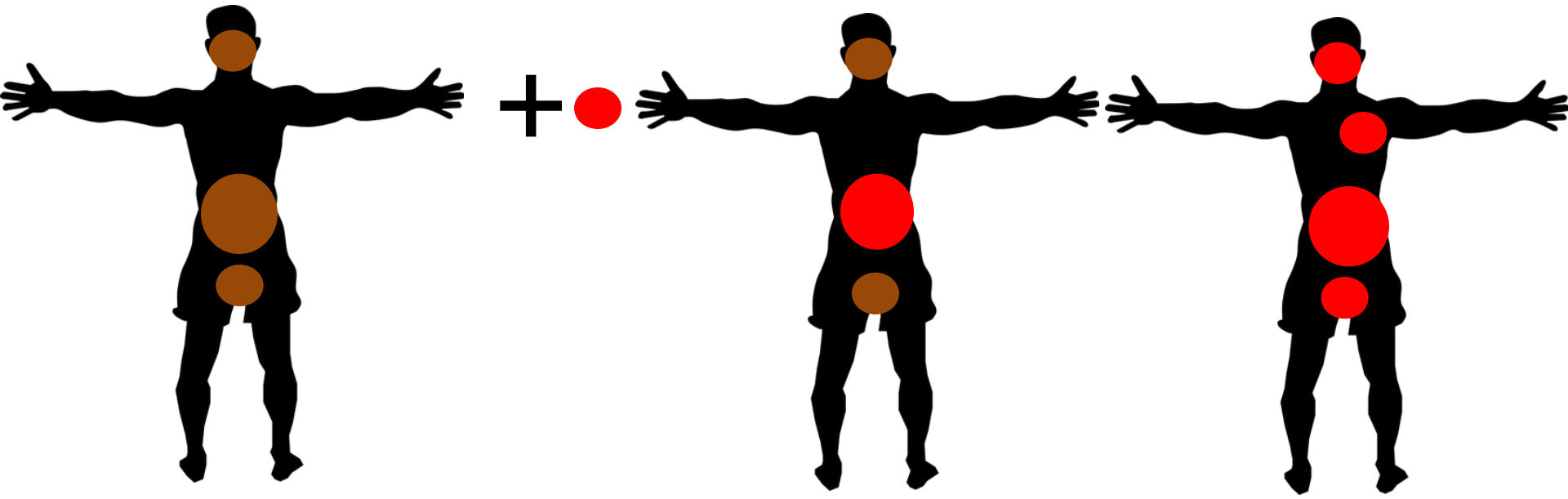
6

	Study group (n=16)		Placebo (n=7)	
	Full response	No response	Partial response	Full response
+30	<p>Bacteroides fragilis</p>	<p>Citrobacter spp.</p>	<p>Citrobacter spp.</p>	<p>Kl. Pneum. Bifidobac. spp.</p>
+45	<p>Bacteroides fragilis</p>	<p>Citrobacter spp.</p>	<p>Citrobacter spp.</p>	<p>Citrobacter spp. Kl. Pneum.</p>
+60	<p>Bacteroides fragilis</p>	<p>Citrobacter spp.</p>	<p>Citrobacter spp.</p>	<p>Citrobacter spp. Kl. Pneum.</p>
+75	<p>Bacteroides fragilis</p>	<p>Citrobacter spp. Enterococcus spp.</p>		
+90	<p>Bacteroides fragilis</p>	<p>Citrobacter spp.</p>		

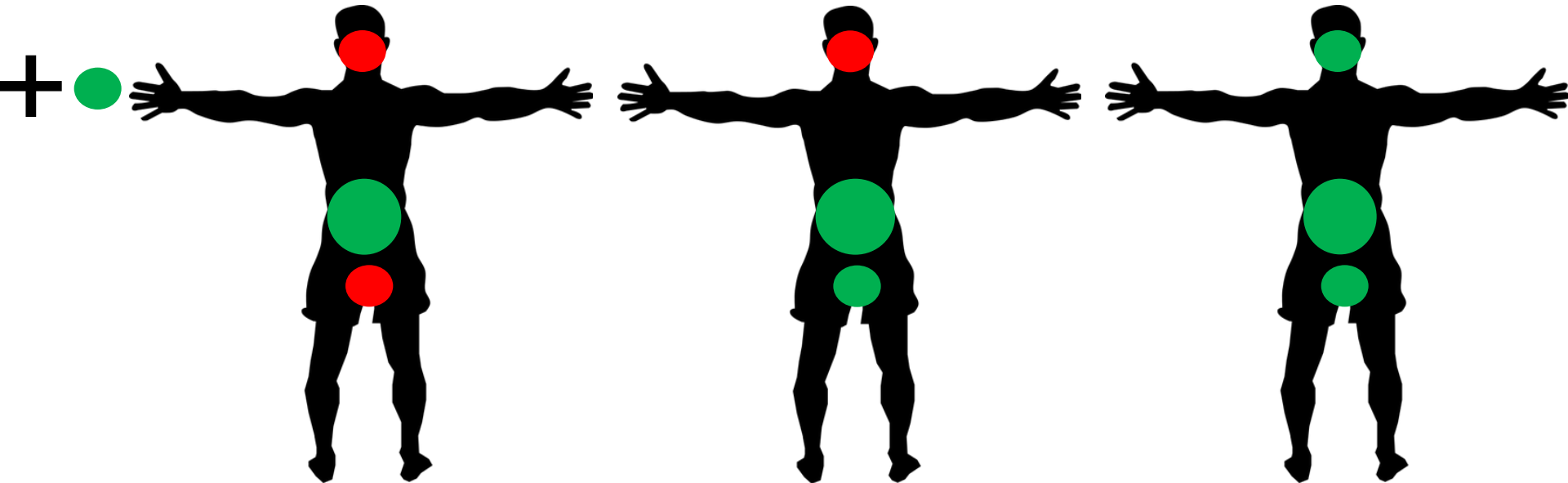
Selective pressure of fecal microbiota - change of microbiota in other loci



Stages of Colonization



Stages Decolonization



Study	Bacterium	Sample	Study group	Placebo	Result	Result
Saidel-Odes, 2012	CRE	20/20	Colistin (1 MIU) + gentamicin	Placebo	28 days	58,5%/33,3%
Nouvenne, 2015	CRE	18/14	High doses of probiotics	Standard therapy	Not specified	53%/12%
Chen, 2014	CRAB	81/54	Colistin inhalation (2 MIU / 160 mg)	Standard therapy	14 days	54%/30%
					28 days	67%/52%
Lubbert, 2013	CRE	16/76	Colistin Sulfate + Gentamicin Sulfate	Spontaneous decolonization	Not specified	57%/83%
Troche, 2005	3GCepHRE ESBL producer	37/0	Colistin Sulfate + Neomycin + Erythromycin		Not specified	46%

FMT studies in HSCT recipient for restoring gut microbiota and eradication of antibiotic resistant bacteria

Study	Indication	Number of patients	Administration route	Study type	Donor relation	Total N° of FMT's	Adverse Events	Response /Endpoint
Bilinski et al., 2017	Multidrug-resistant bacteria decolonization	20 (n=8 allo-HSCT recipient; n=12 other hematologic conditions)	Naso-duodenal tube	Prospective	Unrelated	25	No serious AE's	15/20 decolonization of multidrug resistant bacteria
DeFilipp et al., 2018	Gut microbiota reconstitution following allo-HSCT	13	Oral capsules	Prospective	Unrelated	13	1 abdominal pain	Improved microbiome diversity
Taur et al., 2018	Gut microbiota reconstitution following allo-HSCT	25 (n=14 received auto FMT; n=11 no intervention)	Enema	Randomized controlled trial	Autologous FMT	25	No serious AE's	Restored gut microbiota to pre allo-HSCT state
Battipaglia et al., 2019	Multidrug-resistant bacteria decolonization	10 (n=6 after allo-HSCT; n=4 before allo-HSCT)	Enema / nasogastric tube	Retrospective	Unrelated /relative	13 (n=9 after allo-HSCT)	No serious AE's	7/10 decolonization of multidrug resistant bacteria

“Decolonization of *Klebsiella pneumoniae* by the TFM method”

n=5

Характеристика пациентов

Возраст	33(18/49)	м-3, ж-2
Диагноз	n	%
М.М.	1	20
ОМЛ	1	20
МДС	2	40
ОЛЛ	1	20
Вид ТГСК		
а.н.	4	80
Перед ТГСК	1	20
Кондиционирование		
Флюдарабин+Бусульфан	3	60
Флюдарабин+Циклофосфан+Цитарабин	1	20
нет (терапия Блинатумомабом)	1	20
Проф.РТПХ		
Циклофосфан+Такролимус+ММФ	3	60
Такролимус+ММФ+Бендамустин	1	20
нет	1	20
РТПХ ЖКТ	4	80
Терапия РТПХ		
Руксолитиниб	4	80
День ТФМ после ТГСК		
ТГСК Д+94(61/115)	4	80
Д+28 после терапии Блинатумомабом	1	20
Результаты терапии РТПХ		
Полный ответ	2	50
Частичный ответ	2	50
Метод ТФМ		
Замороженные карсулы	5	100
День наблюдения от ТФМ		
146(129/157)		
Исход		
Жив	5	100
Умер	0	0

Inclusion criteria

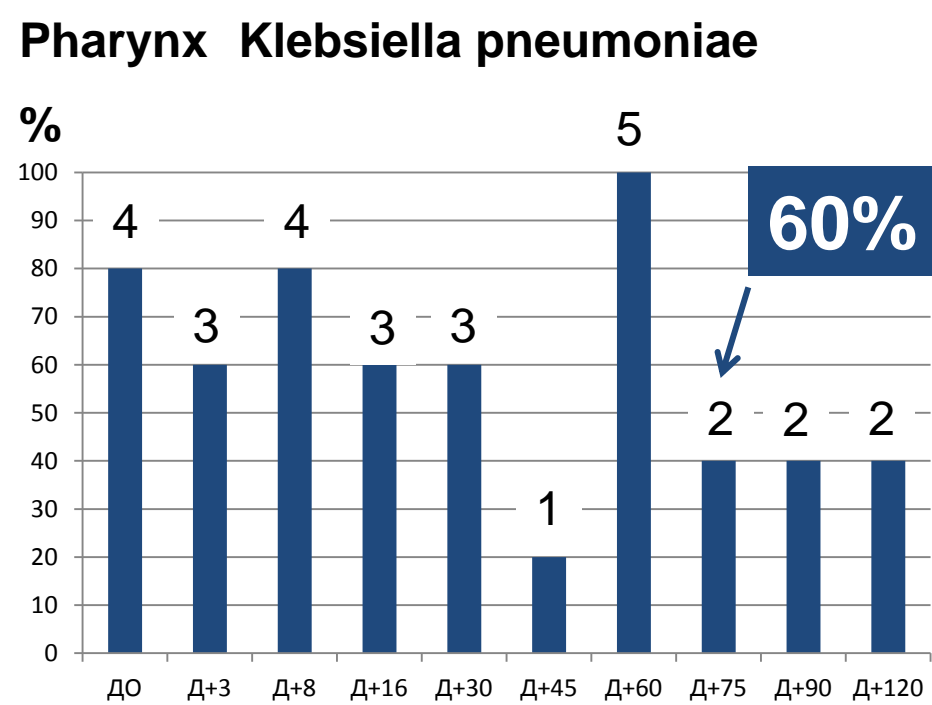
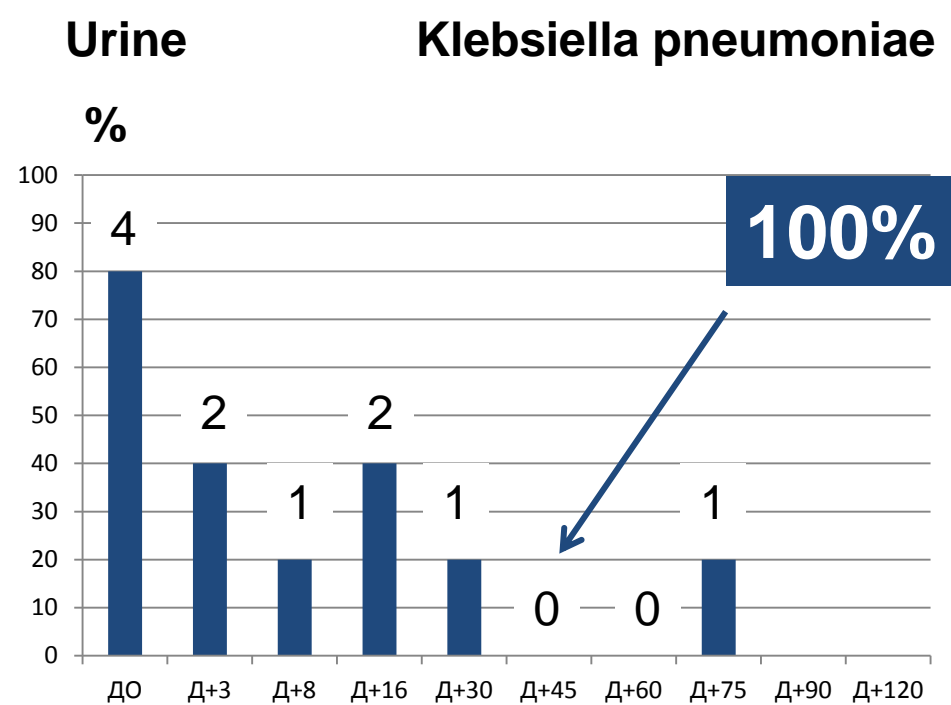
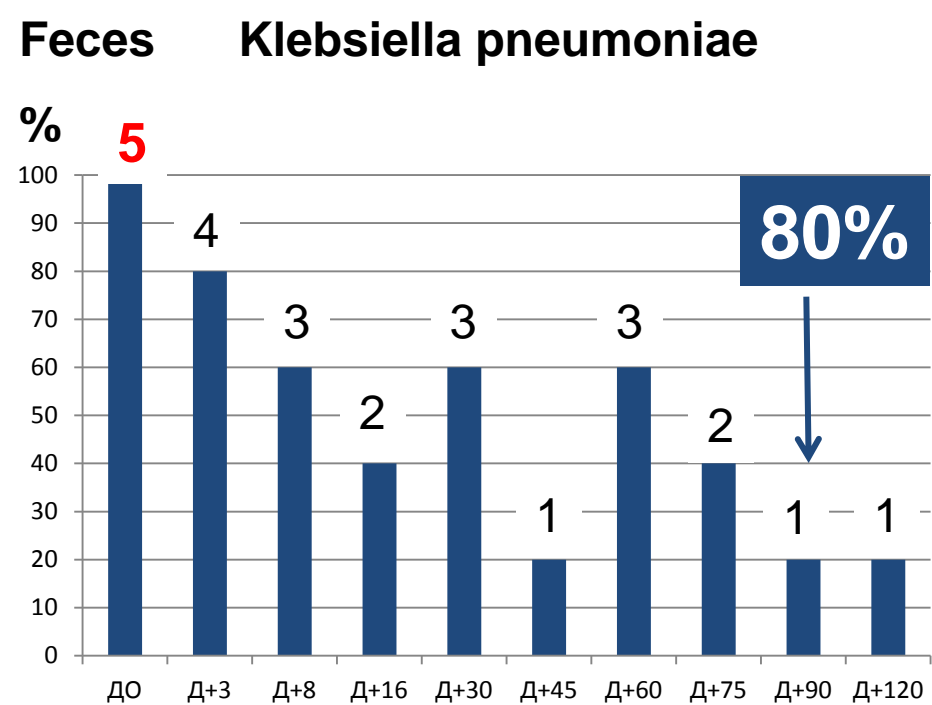
- 18 years
- Colonization *Kl.pneumoniae*-Feces

Research methods

- 1-Cultural method
- 2-Sensitivity to AB
- 3-Detection of carbapenemases by PCR method "AmpliSens® MDR Carbapenemase type KRS, OHA-48, VIM, IMP, NDM

Study days

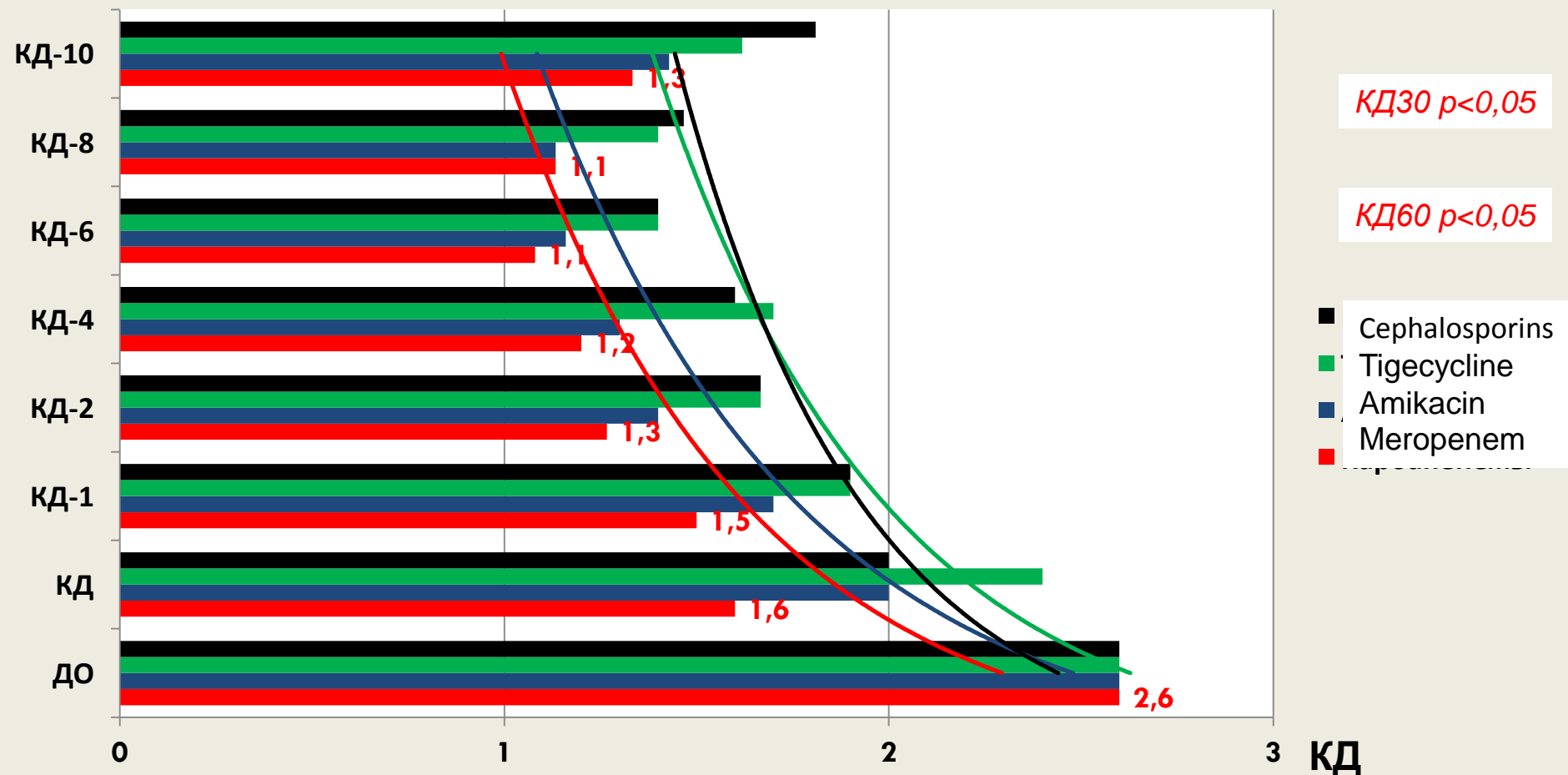
Before FMT
D+3, D+8, D+16, D+30, D+45,
D+60, D+75, D+90, D+120



Feces Increased colonization, increased antibiotic resistance

K. pneumoniae

n = 5 patients after FMT

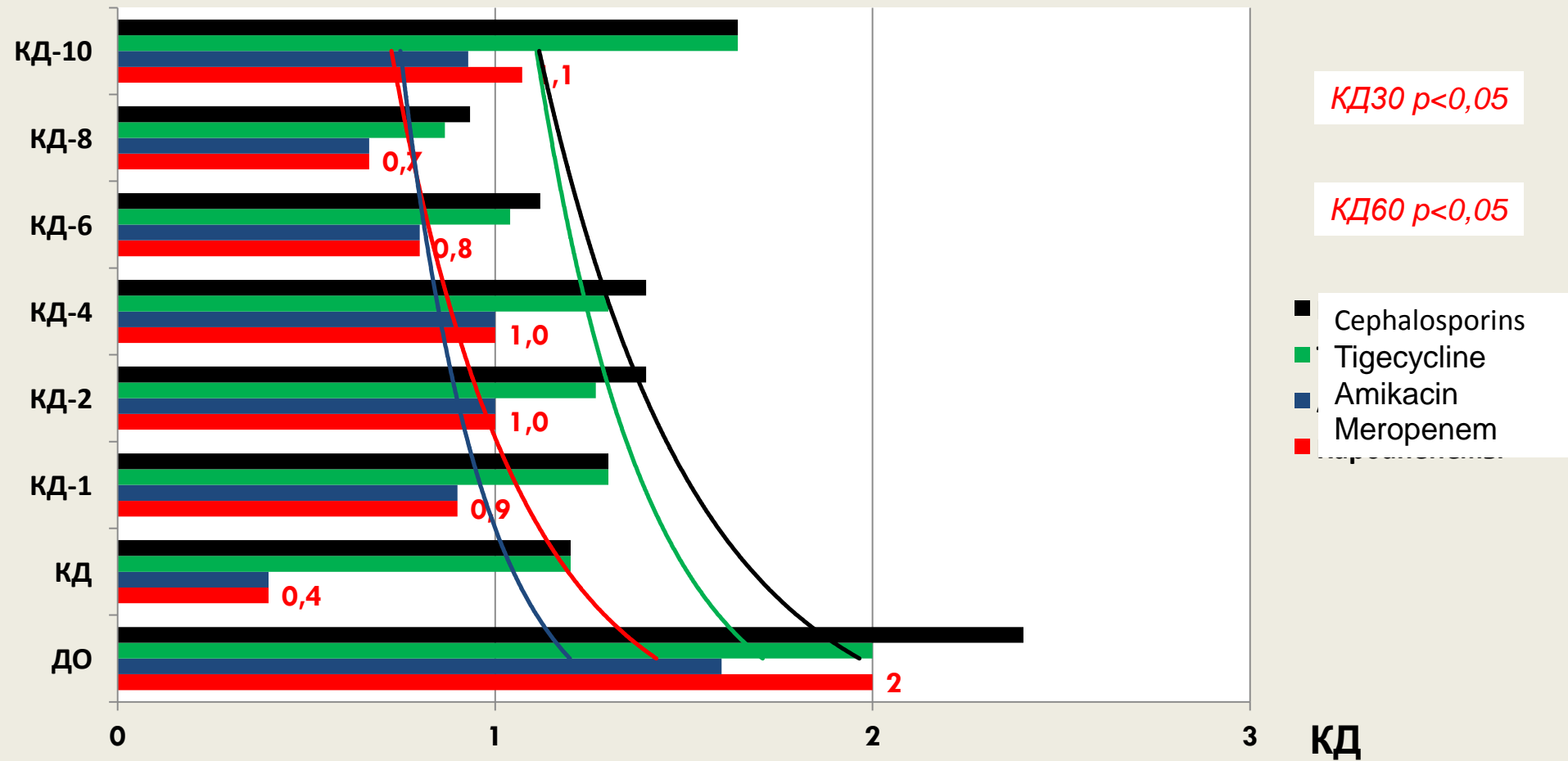


Urine

Increased colonization, increased antibiotic resistance

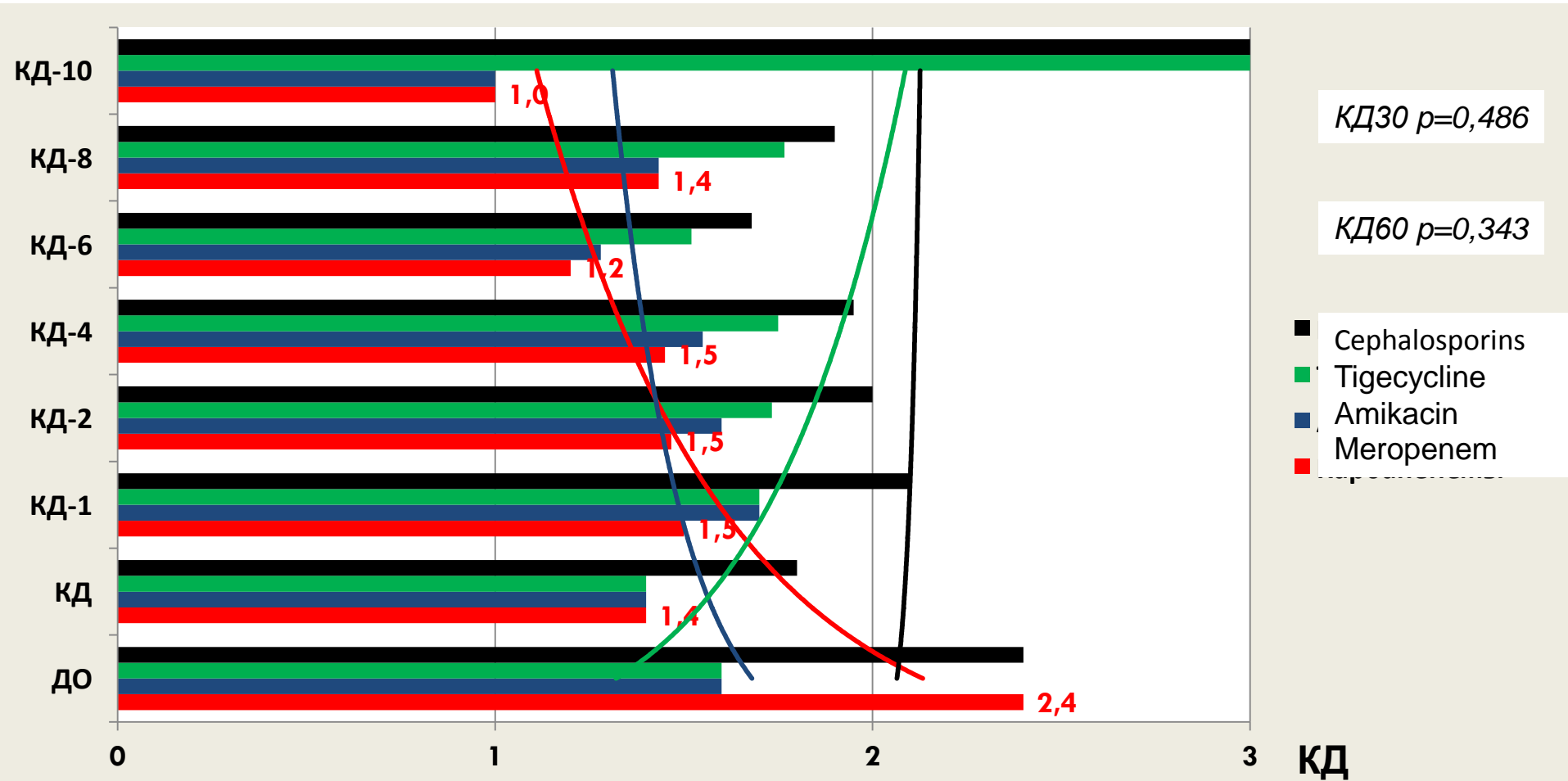
K. pneumoniae

n = 5 patients after FMT



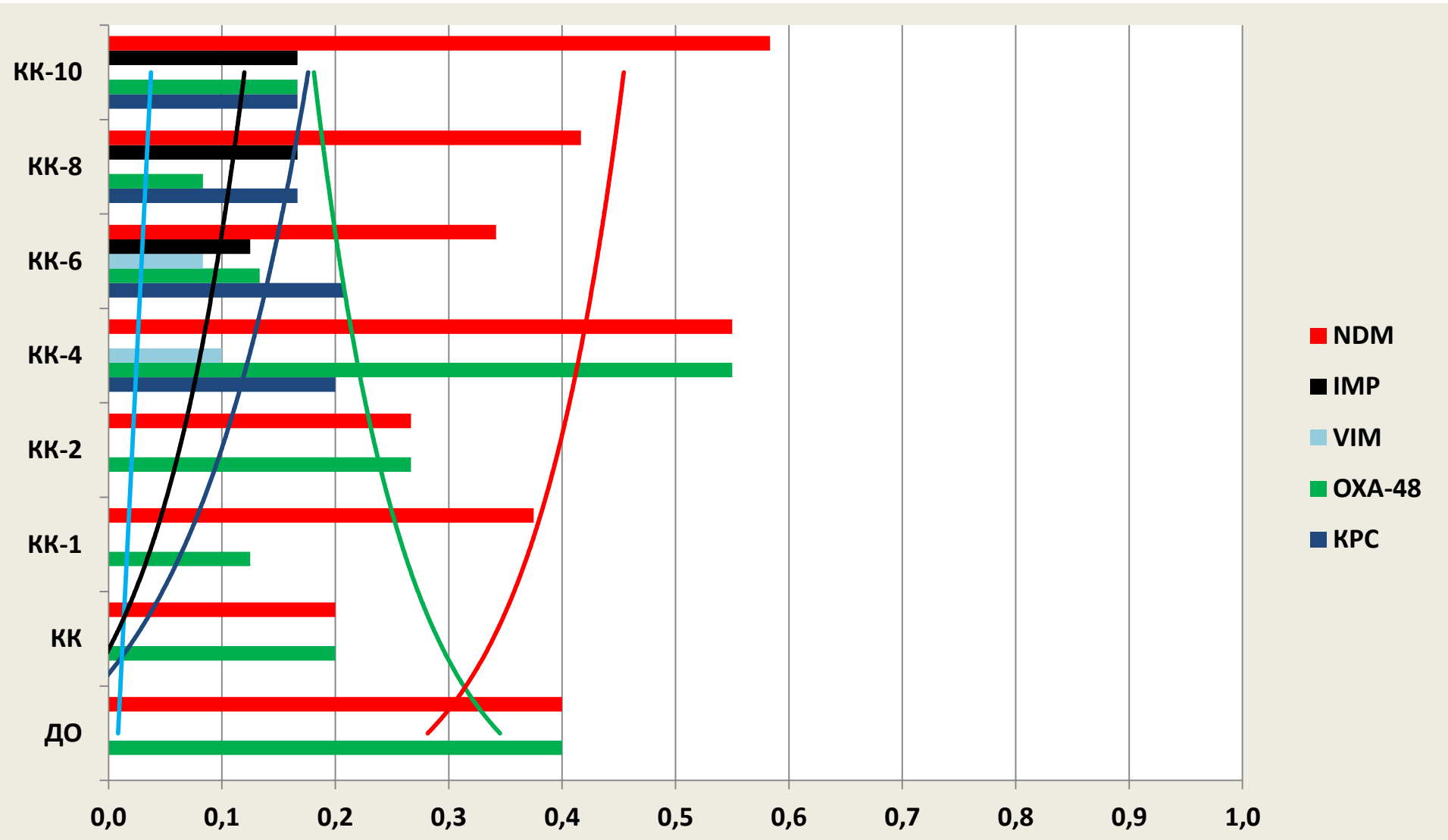
K. pneumoniae

n = 5 patients after FMT



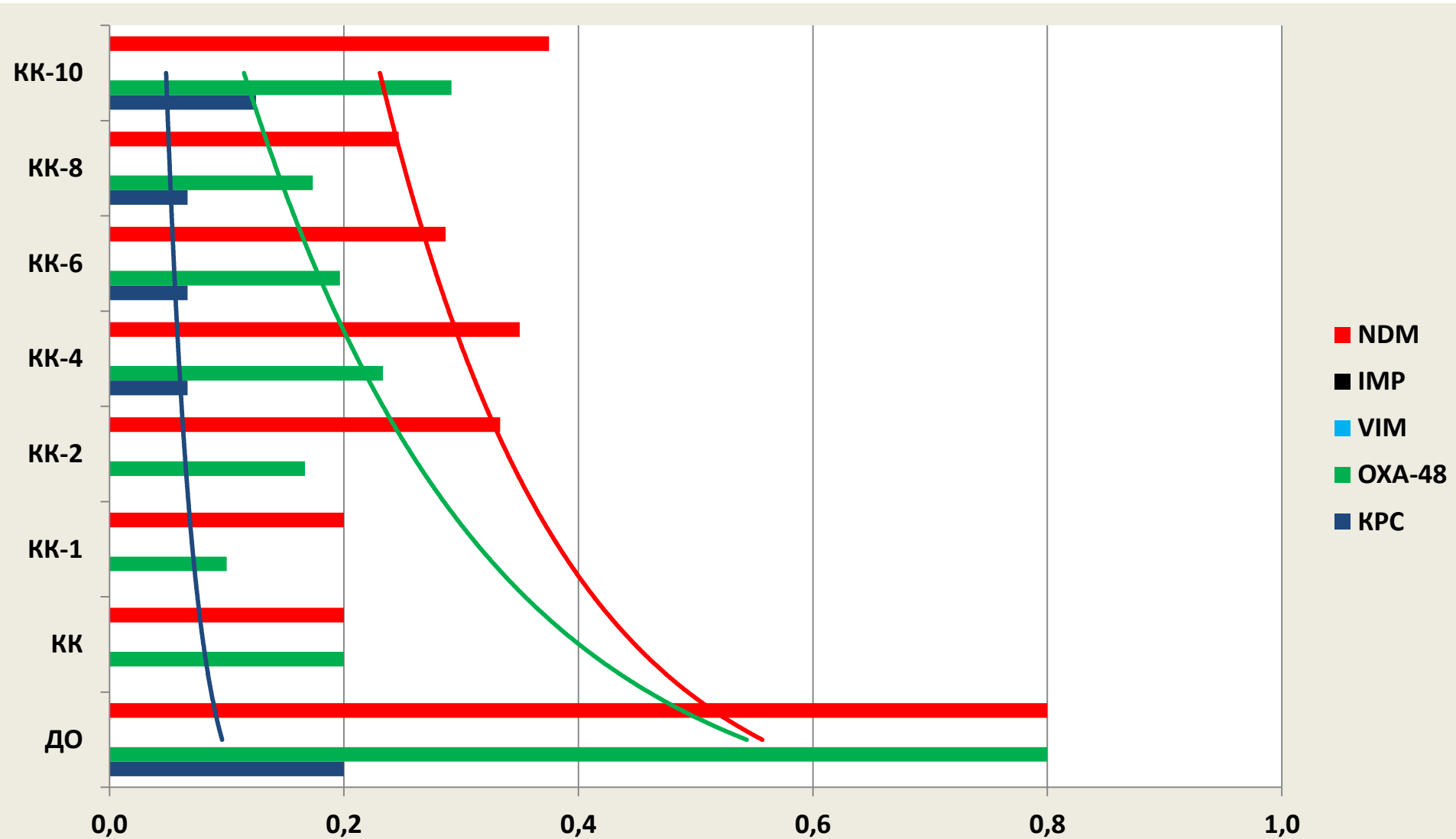
Colonization by Carbapenemase Producers

n = 5 patients after FMT

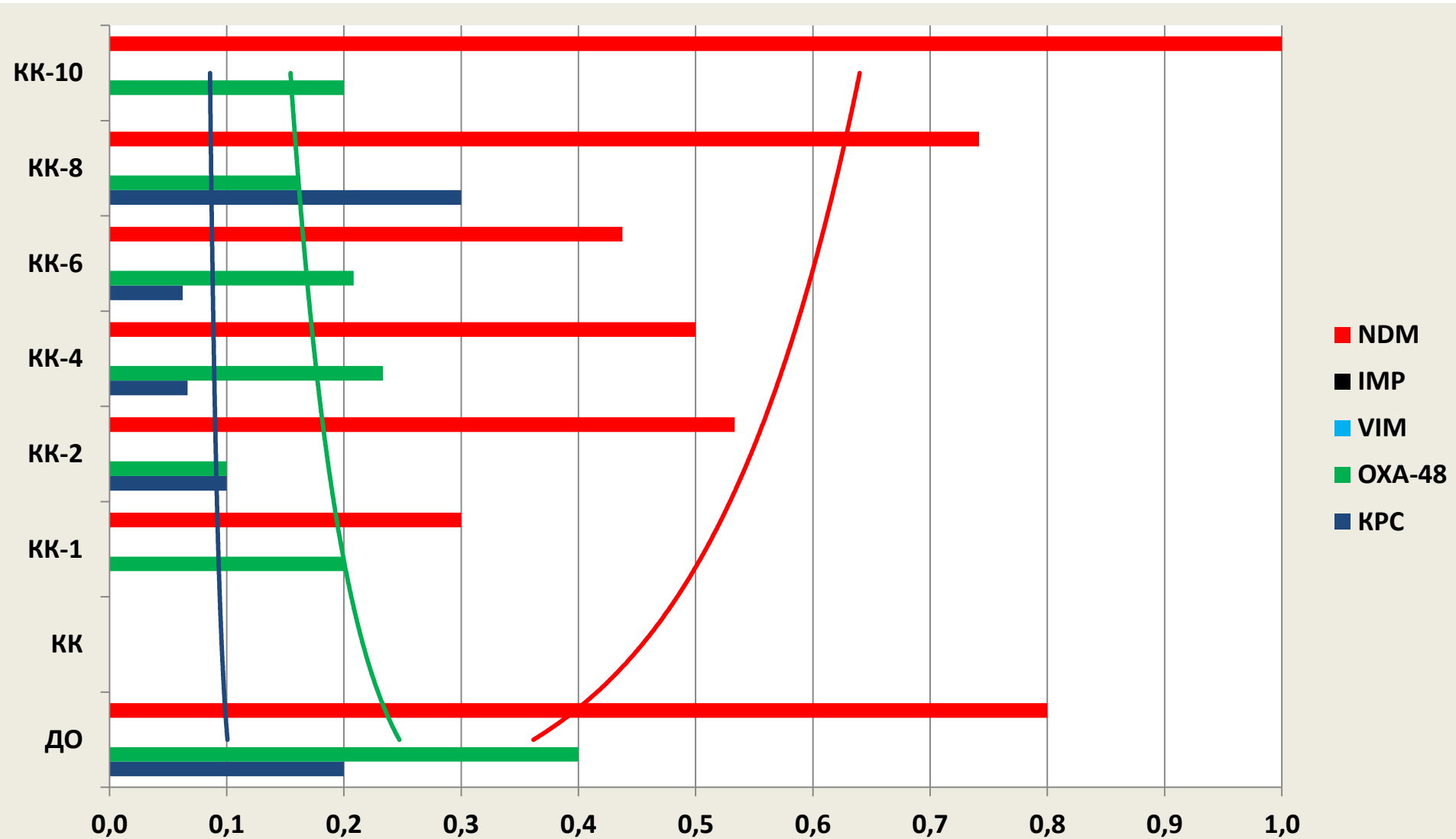


Urine *Colonization by Carbapenemase Producers*

n = 5 patients after FMT



n = 5 patients after FMT



Conclusions

- 1 – FMT – is effective treatment option for GVHD GIT (Complete response 64%)
- 2 – To avoid "hospital" donors of FM and donors with "features" of a diet
- 3 – PCR stool analysis data after TFM can be a confirmation method of engraftment, changes in the intestinal microbiota
- 4 – FMT - can be considered as a method of biological decontamination of gastrointestinal tract in patients after HSCT
- 5 – Sepsis and intestinal bleeding in patients after HSCT are not absolute contraindications to FMT
- 6 – Rational antibiotic therapy - not contraindicated in patients after FMT
- 7 – FMT can be considered in patients after HSCT, as a method of treatment for *Clostridium difficile* infection
- 8-TFM can be used as a method of biological decolonization, restoring the sensitivity of *Klebsiella pneumoniae* carrying genes of resistance to carbapenems and aminoglycosides

Thank you for your attention



In the Philippines!

In Russia!

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