

1. Idea and purpose of the game

Players represent a group of individuals in the population with specific characteristics regarding the oral microbiome and lifestyles. As the game progresses, various events will modify this microbiota. Concomitantly, research activities carried out through projects such as **Stick out your tongue** will discover new aspects of the microbiota and study more populations.

The "Stick out your tongue" project aims to study the microbial composition of the oral cavity and how it changes according to various variables, such as lifestyles. In addition to studying the general population, including people of all ages from various locations in Spain, the project has a specific focus on people with cystic fibrosis, celiac disease and Down's syndrome.

Over the course of five rounds, players must cooperate with each other in order to achieve an oral microbiota as balanced as possible by the end of the game. When working together, players should decide who assumes certain imbalances and when is the best time to undertake the positive actions that are available to each player.

WATCH OUT! The players do not compete with each other to see who wins, but collaborate for a common goal. This means that during the game some players will sacrifice more than others to achieve the best result for the team.

2. Components

20 large cards:



10 representing individuals



10 for Characteristics

56 standard cards:



34 for Events (problems, life goes on, ...)



22 for Actions (daily activities, research results)

For 5 players

- 37 dice: genus: 31 white infection: 6 black
- 12 severe condition tokens

For 4 players

30 dice: genus: 25 white infection: 5 black

10 severe condition tokens

For 3 players

23 dice: genus: 19 white Infection: black

8 severe condition tokens

3. Game Components

Individual and characteristics cards



The **Individual Cards** represent individuals (child, teenager, adult and elderly) and make up half of our character. Each card has five boxes on which dice will be placed at the beginning of the game (as we will explain later). Each box represents a bacterial genus present in our mouth (except for *Candida*, which is a fungus) and has a colored background. The dice on each box, which we call the *genus dice*, represent the abundance of that bacterial genus at each point in time. Next to the box there is a number that indicates the target balance of this die. When this number coincides with the value of the die, that genus is optimally balanced within the oral microbiome. During the game, various events will throw your microbiome out of balance (that is, they will change the value of the dice).

These individual cards also have one, two or three **round boxes** to place the **severe condition (SC) tokens** in case you receive them during the game.

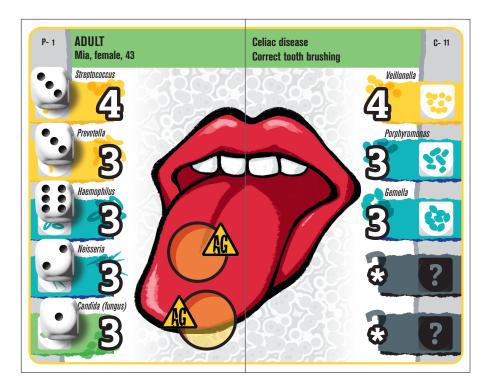


The **Characteristics Cards** make up the other half of your character. These cards include three boxes for genus dice and two black background boxes for the **black infection dice**. At the start of the game all these boxes are empty and only receive dice when a card indicates so, usually with the expression "You discover..." (or during infections, as you will see).

Note that the background colour of several genera is the same. The color groupings correspond to genera observed during the study with common characteristics. For example, the study *Stick out your tongue* found that in the mouth, bacterial flora is organized into different types of communities or *stomatotypes*, with similar microbial composition. Stomatotypes indicate different microbial ecosystems. In our study, we found two main stomatotypes, one with higher proportions of the genera *Neisseria* and *Haemophilus*, the other with higher proportions of *Prevotella* and *Veillonella*.

IMPORTANT! Whenever you talk about the color of a dice, you should refer to the color of the box in which the dice are placed. Whenever a color is mentioned, it refers to any dice of that color (whichever the player wants). For example, refers to any blue dice: either *Haemophilus* or *Neisseiria* or (if the player has them) *Porphyromonas* or *Gemella*. In contrast, for a dice of a particular genus, we always name it specifically; thus, "*Prevotella*" refers to the yellow die of *Prevotella*.

Once the setup of the game is completed (see below), a player's character should look like:



Action and events cards

While **action cards** represent beneficial effects for the players, **event cards** can be beneficial or detrimental, usually the latter. Action cards can be received by the players at the beginning of each round, and they are always intended to benefit other players, never the player himself. Event cards will appear in each round, each time affecting a different player. Players can and should discuss which action cards are best for each of them.

Generally, all these cards will force the player to change the value of the genus dice (which can be good or bad), to receive additional genus dice (beneficial), to receive black dice (detrimental) or to receive severe condition tokens (detrimental).



Image: Stress of the stress

action cards

The dice and the cards



The **genus dice** represent the relative abundance of each bacterial genera.

In microbiome studies, bacterial communities are characterized by measuring the relative proportions of each genus or species. To do this, "molecular samplings" are performed, counting the number of times each molecule has been observed in each bacterial genus. These relative abundances are usually expressed in percentages. To simplify, in this game we express the abundances of each genus from one to six, the values of the dice. The values represented are based on the actual mean values of six types of participants in our study. We average the data of all donors with a given profile (for example, 30-40 year old woman with celiac disease) and normalize their values in the range of one to six.



The **black dice** represent various infections that while not specifically attacking the oral microbiota, they may affect its composition directly or due to the medication prescribed.



The **severe condition tokens** represent conditions which might temporarily or permanently change the oral health of the character.

4. Overview of the game

A game of *Stick out your tongue* lasts five rounds. During each round, players need to follow several steps. Firstly, any player with two or more dice just on the equilibrium value can draw an action card, provided they do not already have one. Next, once the general situation is assessed, the players decide if they will play some action cards to benefit other players. An event card is then revealed for each player, and its effects must be applied. Finally, a last event card is revealed and players have to discuss which player receives (and applies) it. This ends the round and then a new one begins.

Players lose when one of them is about to receive a severe condition token or a black dice and has no box to place it. Players win when they finish the five rounds of the game without losing. The only thing left would be to determine their final score.

Let's look at all this in detail ...

5. Setting up the game

- 1. Randomly deal each player an individual card and a characteristics card (note that some characteristics cards are incompatible with some individual cards; if you receive one of these, draw another).
- 2. From the dice reserve, take 5 white dice per player plus 1 black die, and roll them all. Now, starting clockwise with the oldest character, each player picks one rolled dice and places it in one of the boxes in their individual card (not in the characteristics card) until all players have a dice in each of the five boxes of their individual card (see image on page 3). Finally, one of the players must place the black infection die in one of their black boxes. Who assumes this black dice? Up to you to decide!

REMEMBER: The number next to each box is the ideal equilibrium value you should reach at the end of the game.

REMEMBER: The characteristics genus dice boxes start empty.

You are now ready to start!

6. How to play

A game lasts a maximum of five rounds. If you do not lose any round, the final score is calculated at the end of the last round, to determine the degree of equilibrium achieved.

Each round has three basic steps, follow them in this order:

- 1. Draw action cards.
- 2. Apply action cards, if desired.
- 3. Draw and apply event cards.

Let's look at each step in detail:

A. Draw Action Cards

- In the first round, all players draw an action card.
- In the second and subsequent rounds, only players who have two or more dice in equilibrium and who do not have an action card will draw one card.

B. Apply Action Cards

Players can discuss amongst themselves whether to keep or play some action cards. Considering that each player has only a few cards and that the cards will only impact other players, it is important to assess the situation of the other players and especially if the cards can benefit the player teammates.

If the players decide to use action cards, they will apply them to the target players. The cards that have been applied are discarded, forming a discard pile.

The effects of the cards will be discussed later in the section entitled "Card Effects".

The effects of action cards are based on observations presented in scientific articles and in our study. These effects are often significant correlations (for example, values of *Veillonella* are significantly lower in people who drink very alkaline tap water) but do not necessarily indicate a cause-effect relationship, which should be proved with direct studies (for example, testing in an experiment whether the alkalinity of the culture medium influences the growth of these bacteria).

C. Draw and Apply Event Cards

Next, each player, in turn, draws and applies an event card to oneself, until all have drawn and applied one card. Cards applied are discarded, forming a discard pile.

The order of turns is determined by the oldest character: in the first round this is the first player and the others follow them in clockwise order; in the following rounds, the first player will always be the one to the left of the first player in the previous round.

After this, a last card is drawn, and the players must decide to whom it will be applied. Consequently, every round will have a player who receives the effect of two event cards.

Let's see the effects of the action and event cards...

Card effects

In general, cards require you to change the value of the dice (can be beneficial or detrimental) and to receive additional genus dice (beneficial), to receive black dice (detrimental) or severe condition tokens (detrimental). Some have different effects that are explained in the cards themselves. Let's take a look at the four basic effects.

A) Change the value of genus dice. Cards can tell the player to change the value of one or more of their dice by increasing, decreasing, moving away from the equilibrium value, or moving closer to the equilibrium value. For this we use the following icons:



IMPORTANT: Each time a dice with value "1" must be lowered or a value "6" raised, the die is kept at its current value and the player receives a **severe condition token**.

B) Receive genus dice. Cards may indicate that the player receives a new genus die. In this case, the player takes a die from the supply and adds it to their card of characteristics, where stated and with the value stated. If the card indicates to take a die of a certain color but the player already has all the possible dice of that color, they simply ignore this sentence in the card.

REMEMBER! With more dice of the same color, it becomes easier to balance your microbiota, because when an event forces you to change the value of a color, the player can choose which of the dice of that color to change.

C) Receive or eliminate black dice. Cards may indicate that the player receives or removes a black dice. In this case, the player takes the dice from the supply and places it in one of the two black boxes of their characteristics card, with the value stated, or they withdraw it from their characteristics card.

IMPORTANT. If at any time a player is given a black dice but their two boxes are already occupied, you (all) **lose the game** immediately.

D) Receive or remove severe condition tokens. Cards may indicate that the player receives a severe condition token. In this case, you only need to take a token from the supply and place it in one of the boxes in the individual card.

IMPORTANT. If at any time a player has to receive a severe condition token but all their boxes are already occupied, you (all) **lose the game** immediately. REMEMBER that each person has a different limit of severe conditions to endure.



E) Increase the value of the black dice. All event cards, next to their title, have an icon showing a value and a black dice. When a player applies an event card and has some black dice in their card of characteristics, they also must increase their black dice the amount indicated (if they have two dice, he can distribute this amount between the two dice, if desired); if the player has no black die, there is no effect.

If a black die must rise above 6, a **contagion** immediately occurs. In this case, follow these steps:

- The player receives a severe condition token.
- The black die is reset at value 1.
- One of the two adjacent players (whoever the player wants) receives a black die with value 1. IMPORTANT: Children infect the two adjacent players, not just one.

7. Victory or defeat

How do we lose?

All players lose if:

- at any point one of the players has to add a severe condition token or a black die and has no free boxes;
- at any point one of the players has to receive a **black die** and cannot because no black dies are left in the supply.

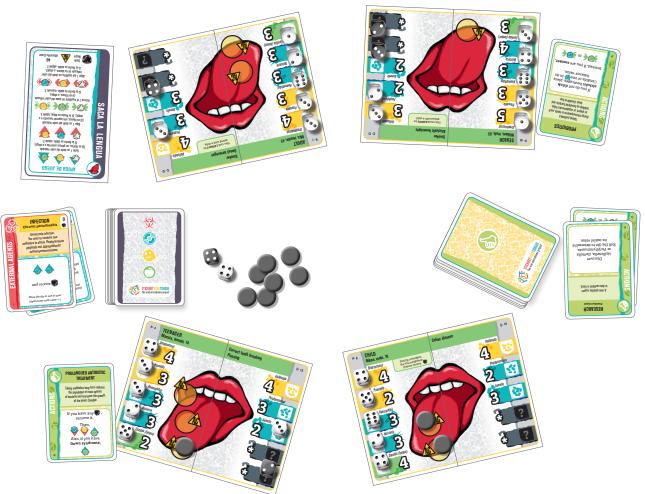
How do we win?

All players win if none of the above situations occur at the end of the fifth round. In this case, you can determine the score of victory, as follows. You have to sum:

- 2 points for each genus die that is at its ideal equilibrium value.
- -1 point for each genus die that is in value 1 or 6.
- -1 point for each black die and for each severe condition token.

The final score categorises your victory as follows:

	5 players	4 players	3 players
Excellent	30 points or more	25 points or more	20 points or more
Good	10 to 29 points	8 to 24 points	6 to 19 points
Acceptable	-10 to 9 points	-8 to 8 points	-6 to 6 points
Needs improver	nent Less than -10	Less than -8	Less than -6



Example: final situation in a four-player game

In this game, players have reached the end of the fifth round without losing, which means that they have won the game and can count their points: 4 black dice = -4 points; 3 SC = -3 points; 5 dice with a value of 1 or 6 = -5 points; 11 dice in equilibrium = 22 points

Total = 10 points, a very good result. Note that Nasir already has two SCs, so if he were forced to receive another one, the players would have lost the game. The same goes for John's black dice.



A game co-created and developed by Marc Figueras, Òscar Oliver, Marià Pitarque, Ivan Prat, (SNAFU) and Elisabetta Broglio (CRG). The illustrations and graphic design are a creation of Bascu. Toni Gabaldón and Jesse Willis (CRG) are the scientific advisors.

The idea originated during a co-creation matinée, held on March 10, 2018 in Vil·la Urània (Barcelona) organized by Elisabetta Broglio in collaboration with Irene Lapuente (La Mandarina de Newton), with the following additional participants: Gemma Agell, Pilar Agustin, Eva Alloza, Nuria Andreu, Victoria Carbó, Laia Cendrós, Francesc Codina, Oriol Comas, Luca Cozzuto, Divya Dadlani, Karel De Pourcq, Marc Figueras, Toni Gabaldon, Julia Gay, William Grace, Sara Gutiérrez Enríquez, Sara Gutiérrez Sanmiguel, Sònia Jario, Maria Lluch, Esther Marín, Margarida Mas, Elisa Mora, Òscar Oliver, Laia Palou, Marià Pitarque, Ivan Prat, Andreu Raig, Luis F. Ruiz-Orejón, Jordi Salvat, Nuria Sanz, Ester Saus, María Vicioso and David Vilalta.

From April to September 2018, many playtests took place at the CRG, in schools and at science-related events in the city of Barcelona (Science Festival, Gutenberg Campus, Research Night, PRBB Open Day). During these events, many people have contributed ideas, most of which have been incorporated into the game. We want to thank and acknowledge the work of all people who have collaborated in the testing phase, especially Gemma Agell, Estefania Aguilar, Eva Alloza, Núria Andreu, Vanessa Balagué, Juan Bascuñana, Martí Cabré, Àlex Caramé, Xavi Cava, Laia Cendrós, Francesc Codina, Luca Cozzuto, Digna Couso, Bruna Domingo, Roger Domingo, Salva Ferré, Pau Figueras, Toni Gabaldón, Toni Garcia, Sara Gutiérrez, Toni Hermoso, Mary Hirschm, Susana Iraola, Sonia Jario, Jonas Krebs, Ewa Ksiezopolska, Irene Lapuente, Gloria Lligadas, Maruxa Martínez, Haridian Montañez, Olga Nabona, Joan Navarro, Francesco di Palma, Andreu Raig, Sonja Reiland, Mónica Rodríguez, David Sastre, Ester Saus, Carlos Sierra, Marta Solís, Jordi Sospedra, María Vicioso, Ada Vilalta and David Vilalta.

Finally, we would also like to thank all the people who donated their saliva for the scientific study (over 3,500 people in two editions); without them, the microbiome results which are the basis of this game would not exist.



A game developed by the CRG in collaboration with SNAFU.





Funders of the project:





illumina eppendorf miniper ThermoFisher



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