

Gut microbiota modulation through antibiotics and fecal microbiota transplantation impacts glioblastoma progression



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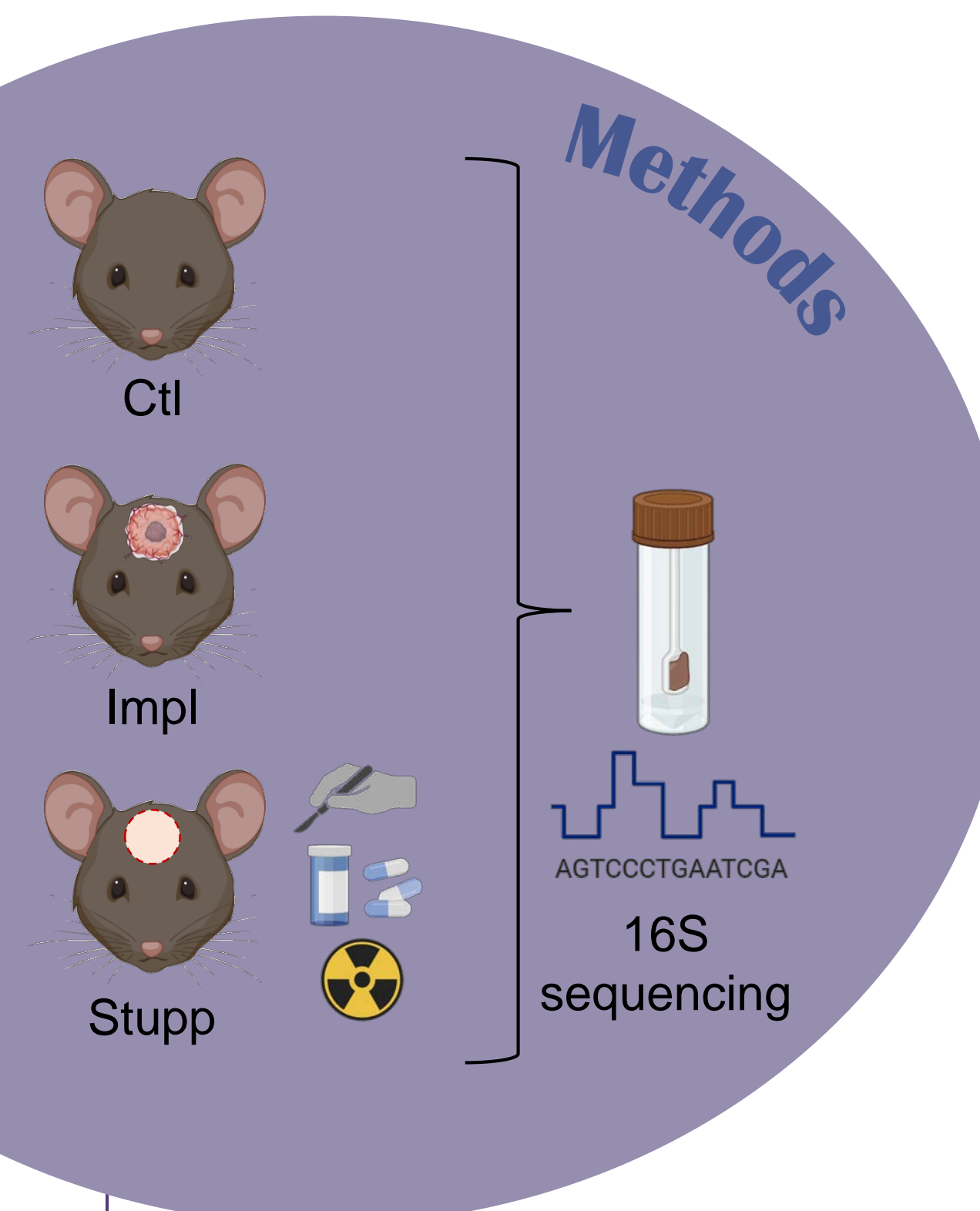


Context

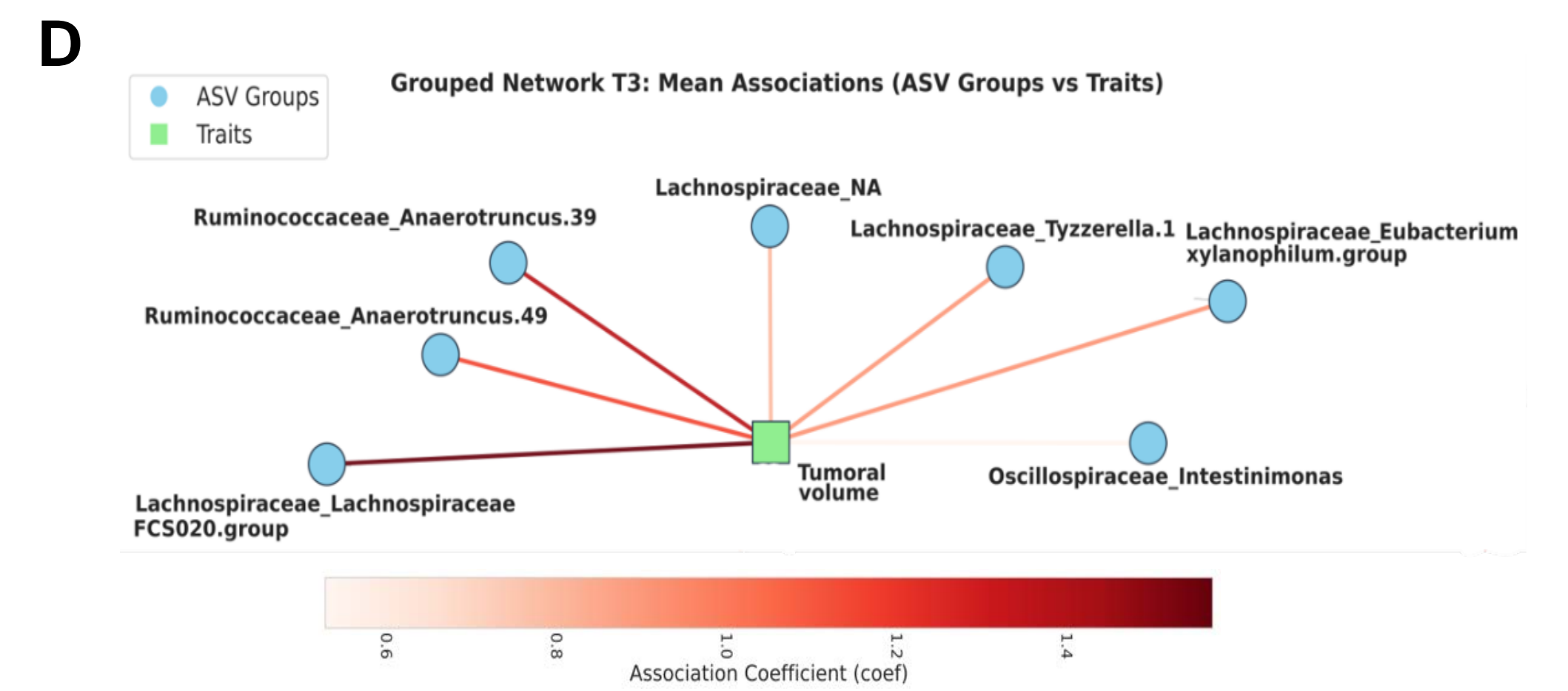
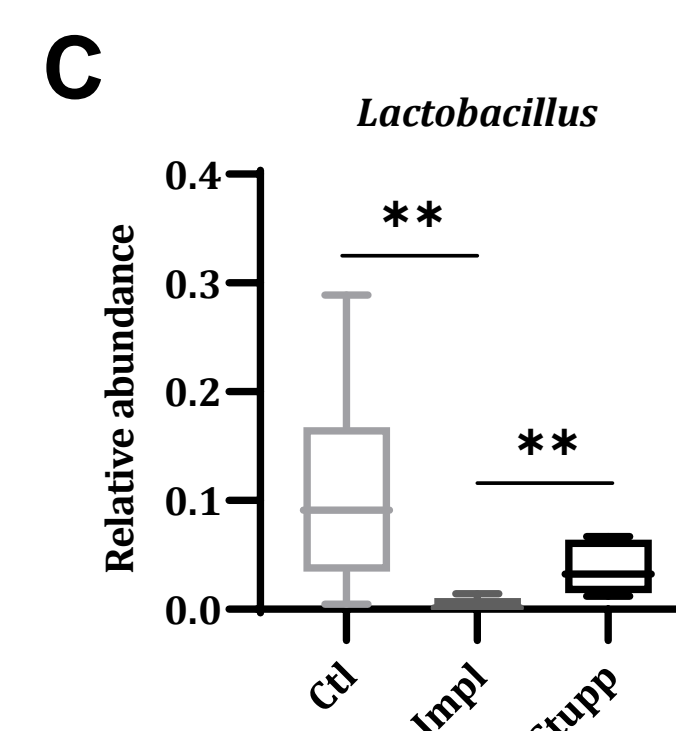
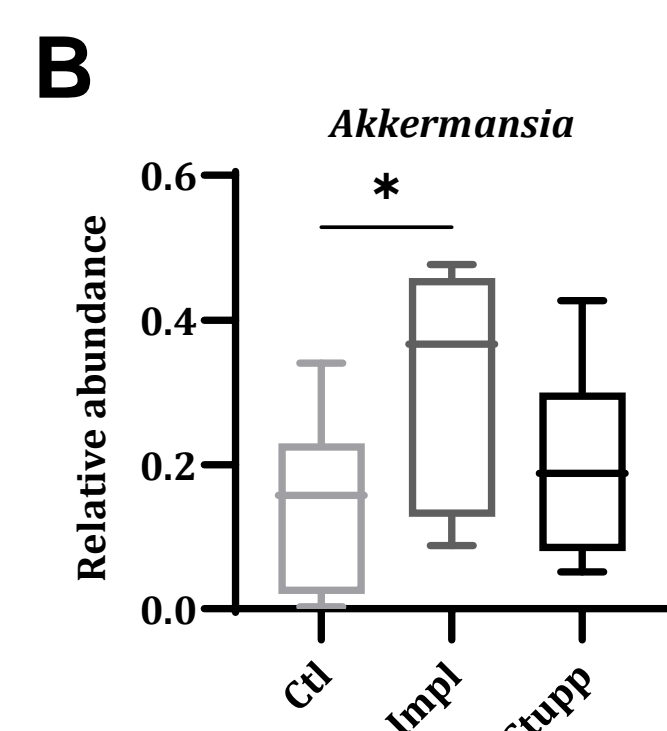
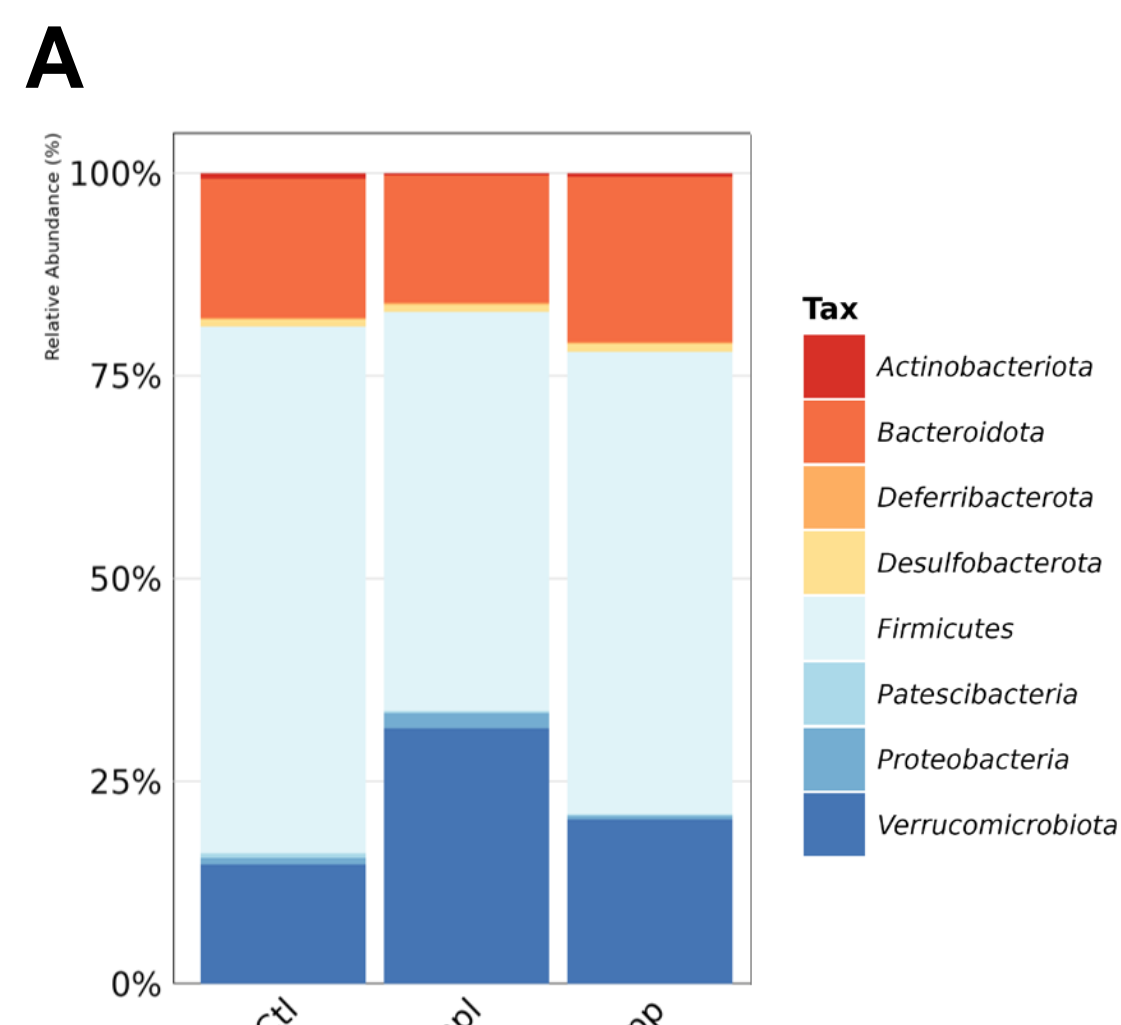
Glioblastoma is the most common and aggressive **brain tumor** in adults, characterized by a poor prognosis, with a median survival of approximately 14 to 15 months and frequent therapeutic failure. To improve patient survival and quality of life, it is essential to identify the factors contributing to the initiation, progression, and therapeutic resistance of this cancer.

In this study, we focus on the gut-brain axis, specifically by exploring the potential role of the **bacterial microbiota**, in glioblastoma progression. The bacterial microbiota refers to the diverse community of bacteria that colonizes the gut, which has been shown to play a crucial role in several brain pathologies, including Parkinson's disease and Alzheimer's disease. More recently, emerging studies have suggested that the bacterial microbiota may influence glioblastoma, but the underlying mechanisms remain unclear.

The main objective of this project is to better understand the role of gut microbiota in glioblastoma progression through its modulation.



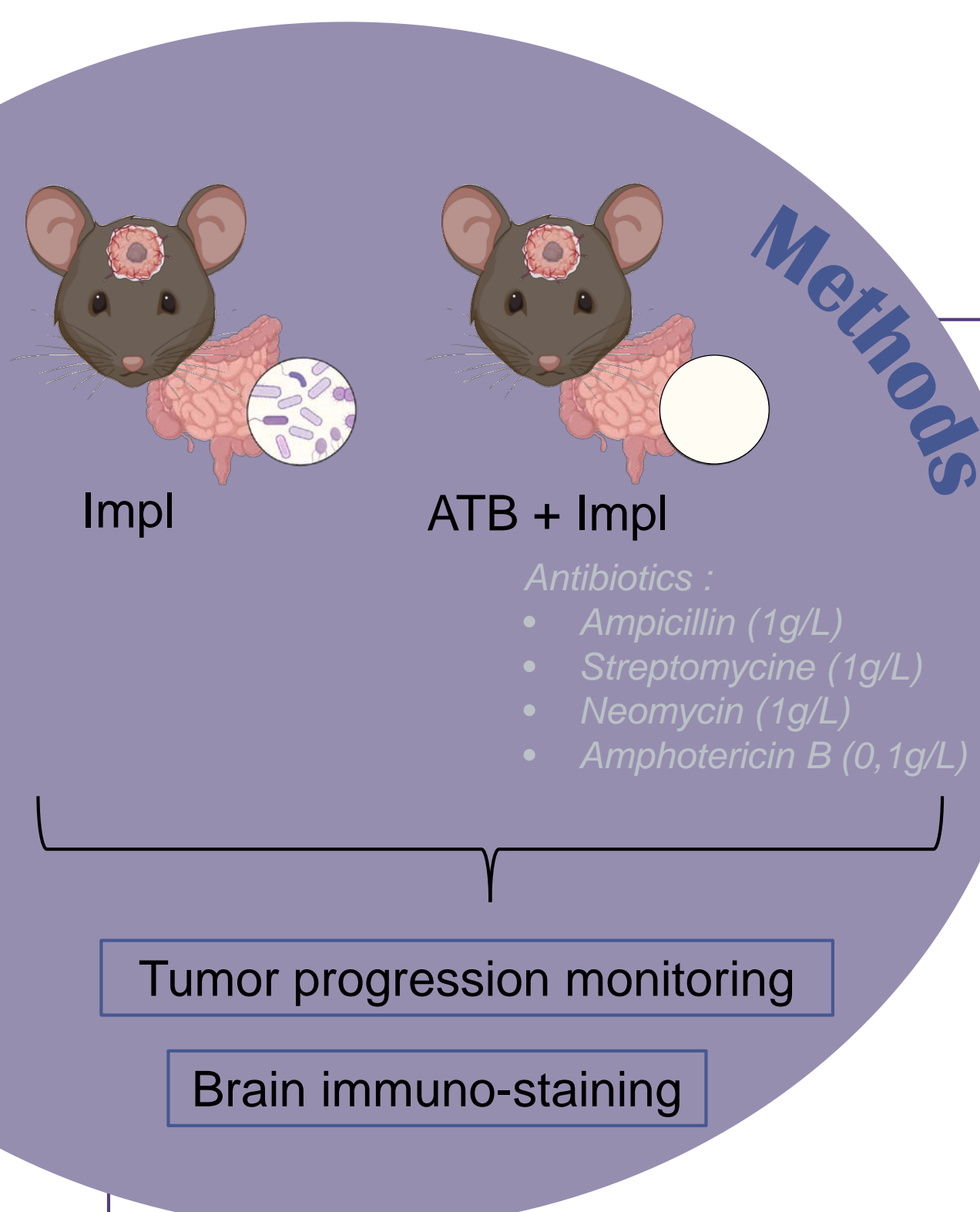
Bidirectional communication between the gut and the brain



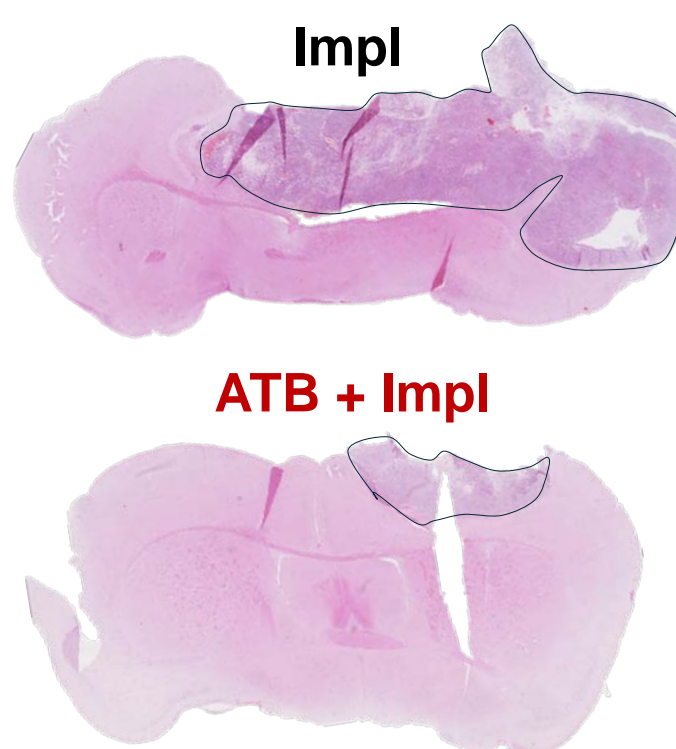
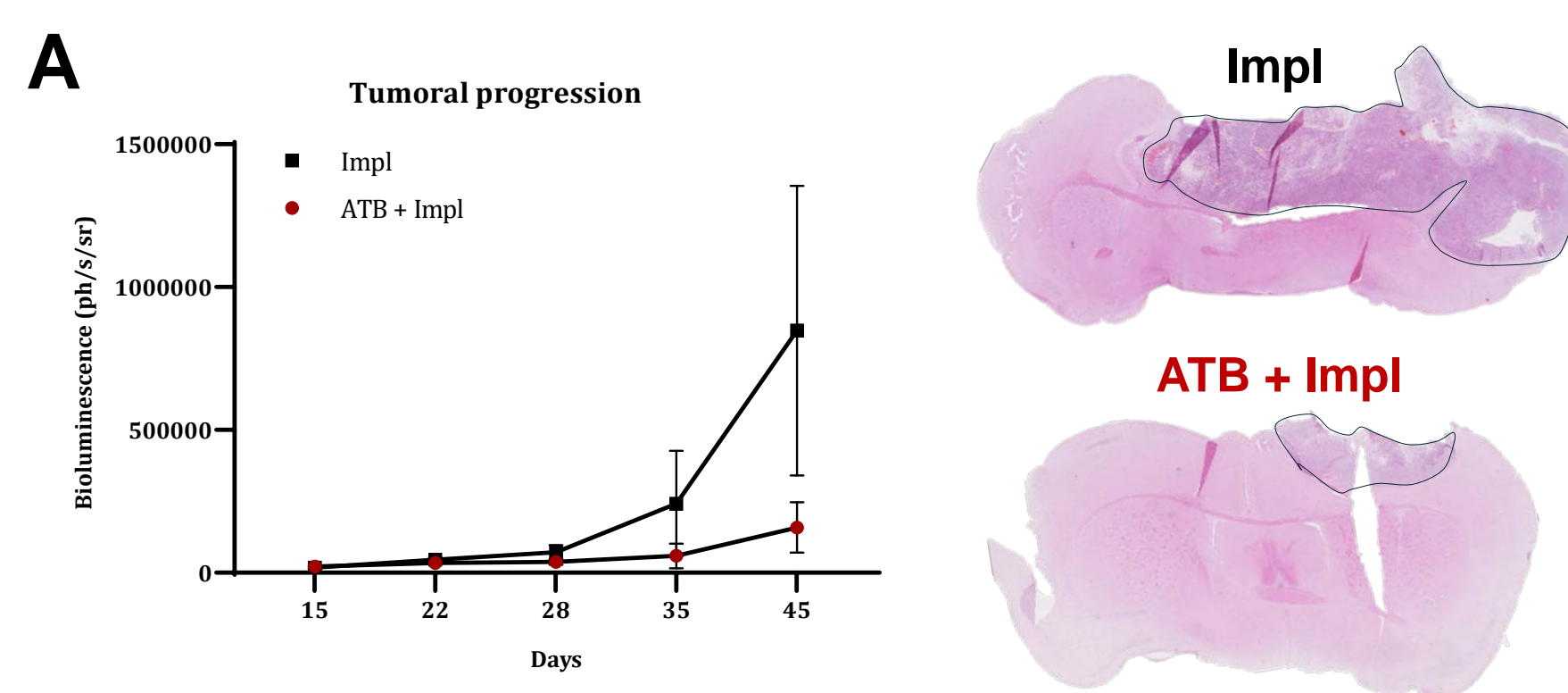
Glioblastoma implantation changes gut microbiota composition

The stupp protocol restores partially gut microbiota composition

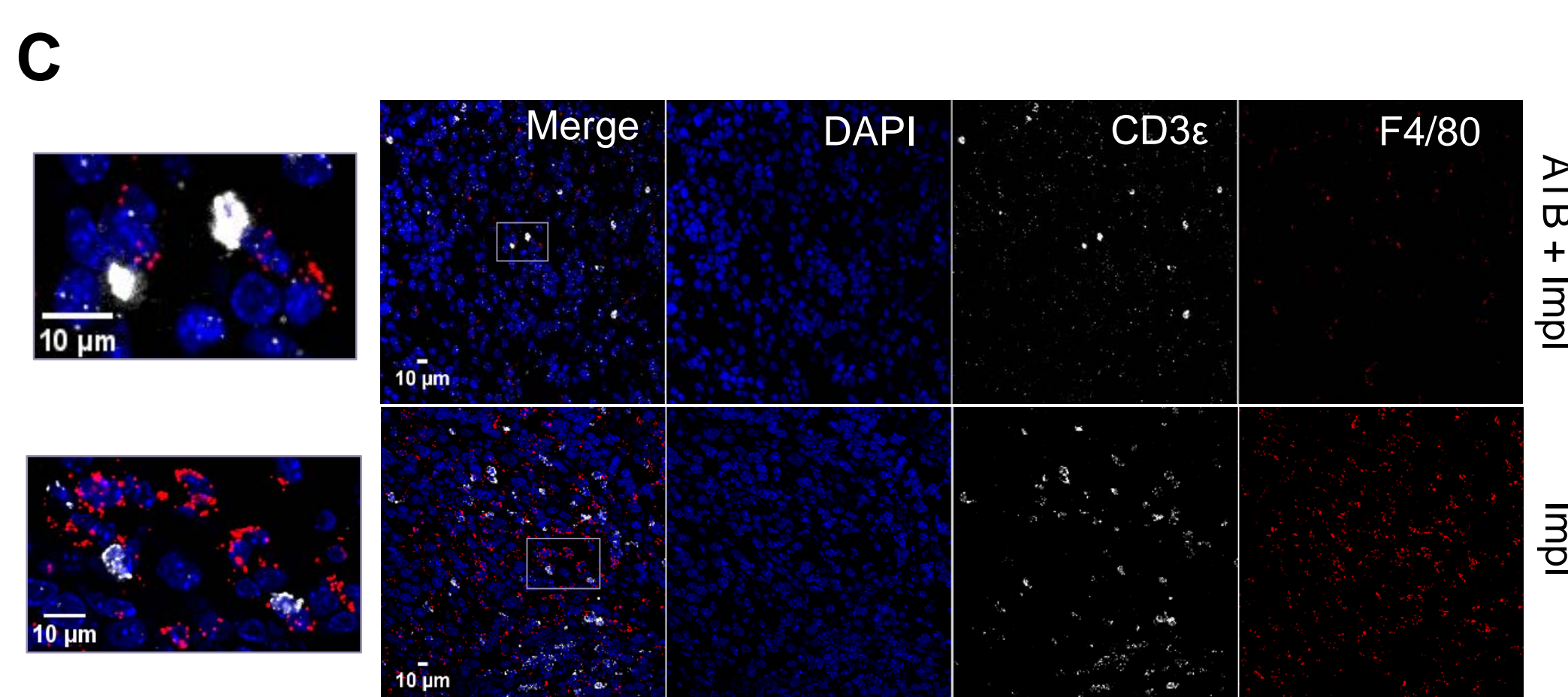
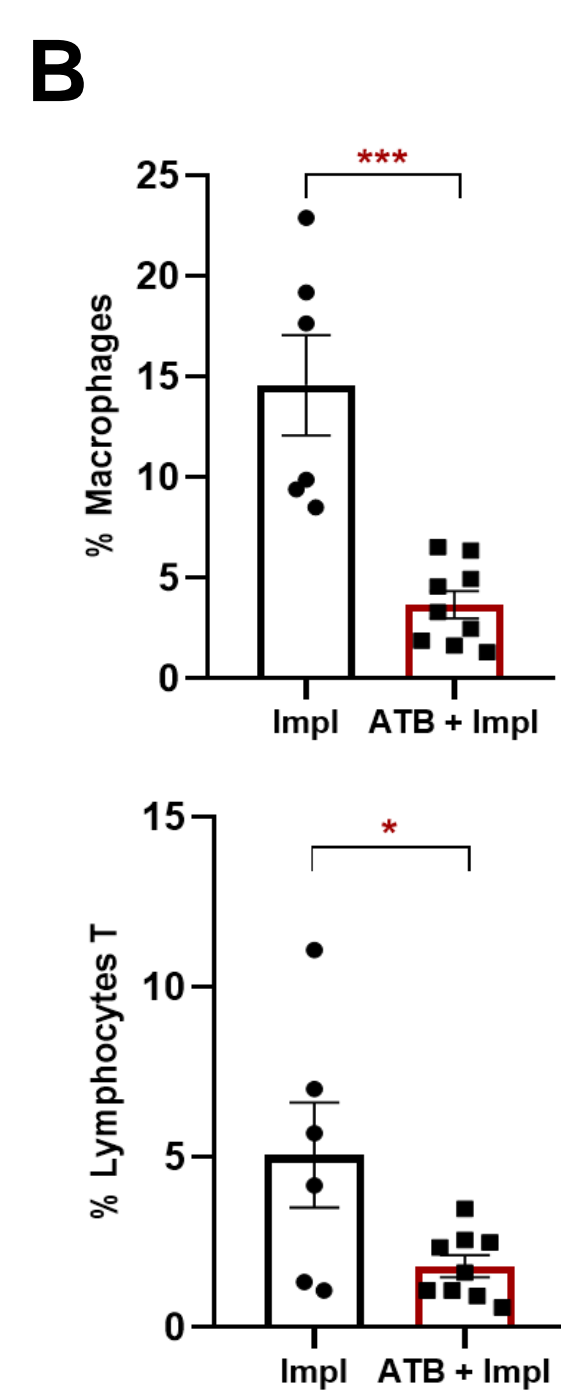
The presence of bacteria from the **Lachnospiraceae** and **Ruminococcaceae** family in the gut is associated with an increased tumor volume



Modulation through antibiotics



Mice without gut microbiota (ATB + Impl) have smaller tumor progression



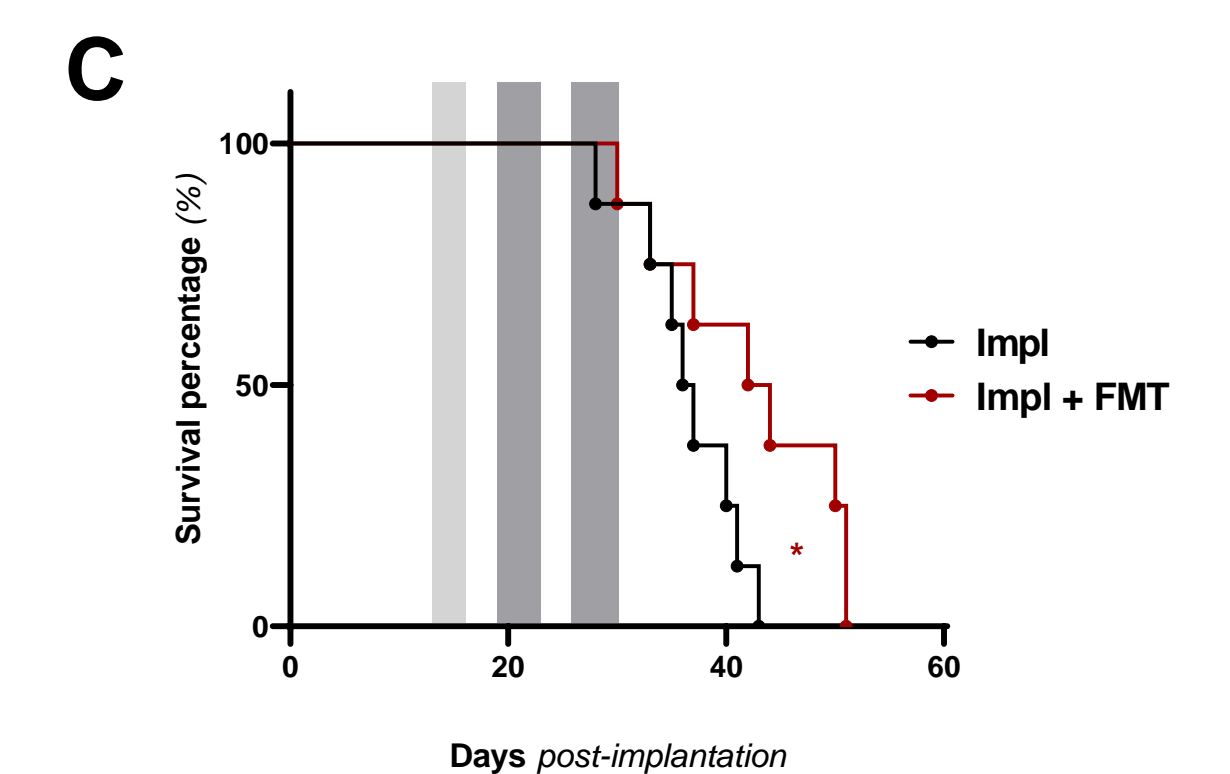
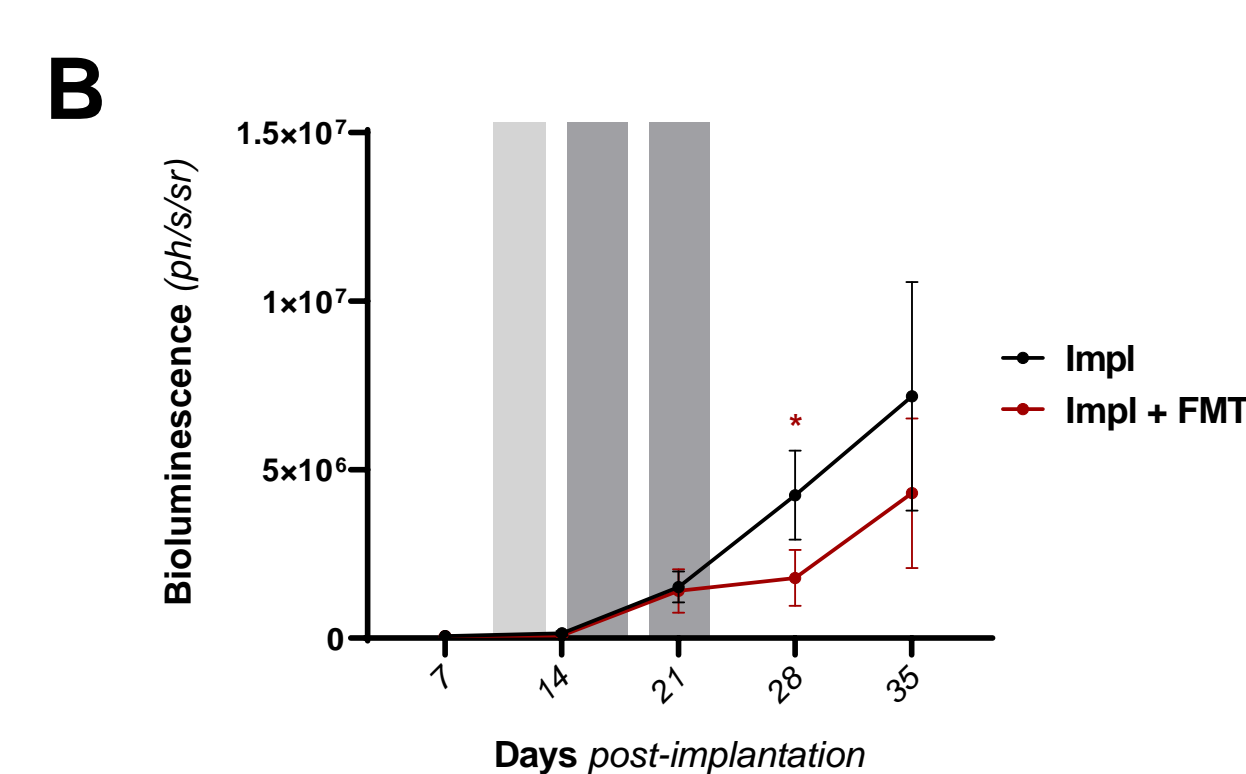
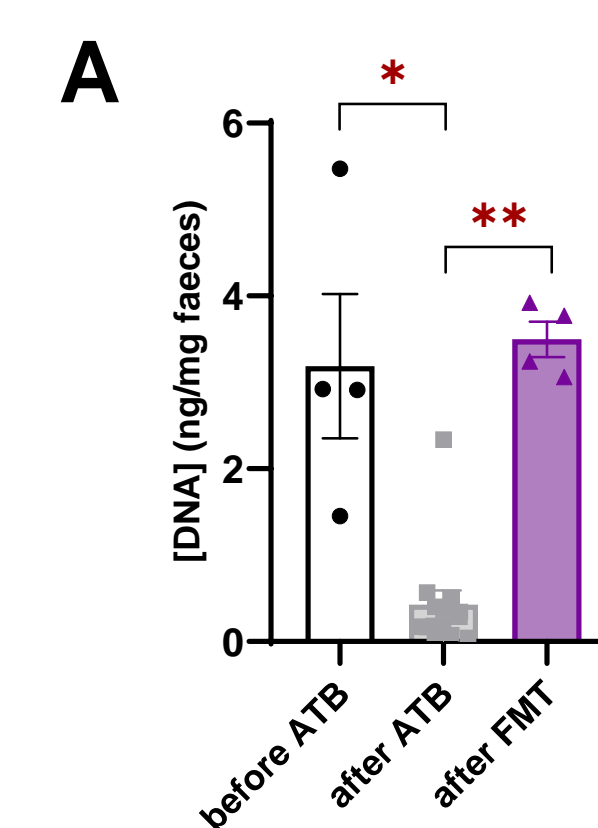
There is significantly less immune infiltration in mice's brain treated with antibiotics

Figure 2 : (A) Evolution of tumoral progression in mice treated (ATB + Impl) or not (Impl) with antibiotics. (B) Percentage of macrophages and T cells infiltrating the tumor of implanted mice treated or not with antibiotics. (C) Representation of immune infiltration within the tumor by RNAscope multiplex technic. T cells are identified by targeting CD3ε gene (TSA 570) and macrophages by targeting F4/80 gene (TSA 650)

Modulation through fecal microbiota transplantation

Gut bacteria are successfully depleted by ATB before FMT

The engraftment of gut bacteria following FMT is validated



Fecal microbiota transplantation (FMT) from healthy to implanted mice :
 • Slows down significantly tumor progression
 • Increases mice survival

Figure 3 : (A) Gut microbiota evolution quantified by qPCR on bacterial ribosomal 16S DNA in faeces before and after antibiotic treatment and after fecal microbiota transplantation (FMT). (B) Evolution of tumoral progression in mice receiving fecal microbiota transplantation (Impl + FMT) or not (Impl) and the survival percentage associated (C).

Take home message

The gut and brain are closely interconnected as glioblastoma implantation induces gut dysbiosis. To better understand the role of gut microbiota in this cancer we explored two ways to modulate gut microbiota :

- Depleting gut microbiota through **antibiotic** administration reduces tumor growth
- Reversing gut microbiota dysbiosis induced by glioblastoma through **fecal microbiota transplantation** increases mice survival and slows down tumor progression

These results suggest that gut microbiota may play a role in glioblastoma progression.

Perspectives

Fecal microbiota transplantation appears as an interesting therapeutic application but yet, further analyses are needed to better understand its role :

- Metagenomic to analyse gut microbiota colonization after FMT
- Blood metabolomic
- Immune infiltration within the tumor
- Barrier permeability (BHE and intestinal)