SAE 33 : TD 3 - Réaliser une figure : outil biorender

Les outils pour réaliser des figures

Sur ce TD, vous allez travailler sur un nouvel outil graphique **Biorender** qui a pour intérêt de proposer des dessins d'outils ou de structures biologiques à utiliser et combiner. Cet outil n'est pas un outil de dessin vectoriel et donc ne permet de garder la qualité du rendu si vous utilisez la figure pour l'agrandir. Il est donc pertinent d'utiliser chaque outil pour son utilisation :

- **Biorender**, spécialisé en biologie permet d'avoir des dessins esthétiques pré-réalisés
- **Inkscape/ adobe illustrator** : Dessin vectoriel. Vous avez intérêt à insérer les photos / images dans inkscape pour les agencer ensuite. Le texte ajouté sur Inkscape supportera mieux l'agrandissement. Cela est particulièrement utile pour les posters notamment.
- **GIMP/adoobe photoshop** : Travailler les contrastes de photo ou leur cadrage.
- **Tableurs** : permettent de réaliser des graphiques. Souvent les graphiques des articles sont à un format peu esthétique ou contiennent plus de données que ce que vous voulez exploiter. Vous pouvez utiliser le logiciel xyscan (TD2 - Modèles en SV) pour extraire les données et ensuite refaire le graphique.

La figure à réaliser

Le schéma graphique d'un article scientifique a pour objectif d'attirer l'attention sur le sujet et doit résumer les messages principaux du texte.

Objectifs de la séance

- Synthétiser les informations scientifiques des fiches bibliographiques dans une figure
- Créer un schéma professionnel pour présentation des travaux scientifiques

A. Avant la séance :

1) Avoir préparé, en TD Résolution de la SAE 31, la bibliographie relative à la thématique individuelle
2) Créer un compte BioRender.
3) Examiner attentivement deux documents de support pour la construction d'une représentation graphique.
   a) Support 1 : Un infographique crée par BioRender expliquant comment résumer un texte de manière graphique. Remarquez la disposition à utiliser, les couleurs, les flèches et les légendes.
   b) Support 2 : Les consignes pour créer un résumé graphique par l'éditeur scientifique « Cell », avec des exemples critiqués de quatre « graphical abstract ».

B. Pendant la séance :

1) Discussion d'un abstract et de sa représentation graphique. (20min)
   a) Commencer par examiner la représentation graphique.

b) Rédiger une phrase décrivant votre perception du schéma observé.

c) Lire ensuite le résumé et comparer votre description avec le résumé

d) Répondre aux questions : Recevez-vous le même message en lisant le résumée et en examinant la figure ? Quels éléments pourraient être améliorés dans la représentation graphique ?

2) Réalisation d'un brouillon de votre figure. (20min)

a) Commencer par rassembler les fiches bibliographiques réalisées sur la SAE 31 et décider si la figure à réaliser regroupera des méthodologies expérimentales (i.e. démontrer les instruments et les conditions de manipulation suite à une hypothèse) ou des conclusions scientifiques (i.e. présenter une figure de revue bibliographique qui regroupe des théories).

b) Définir 1 ou 2 phrases qui résument vos fiches bibliographiques ainsi que le texte construit lors de la SAE31.

c) Consulter les enseignantes pour vérifier les définitions qui doivent apparaitre sur le schéma.

d) Esquisser sur papier le contexte de ce que vous souhaitez représenter et les éléments clés à dessiner. Déterminer les formes, flèches et étiquettes pour clarifier les schémas. Sélectionner les couleurs et polices adaptés.

3) Seulement après avoir un brouillon sur papier, investiguer BioRender et les modèles à disposition pour dessiner votre schéma (50 mn).

a) Se rappeler des éléments indispensables pour son message.

b) Esquisser l'ordre de présentation et la numérotation des événements si c'est le cas.

C. Après la séance :

1) Terminer la figure

2) Remplir le carnet de Bord

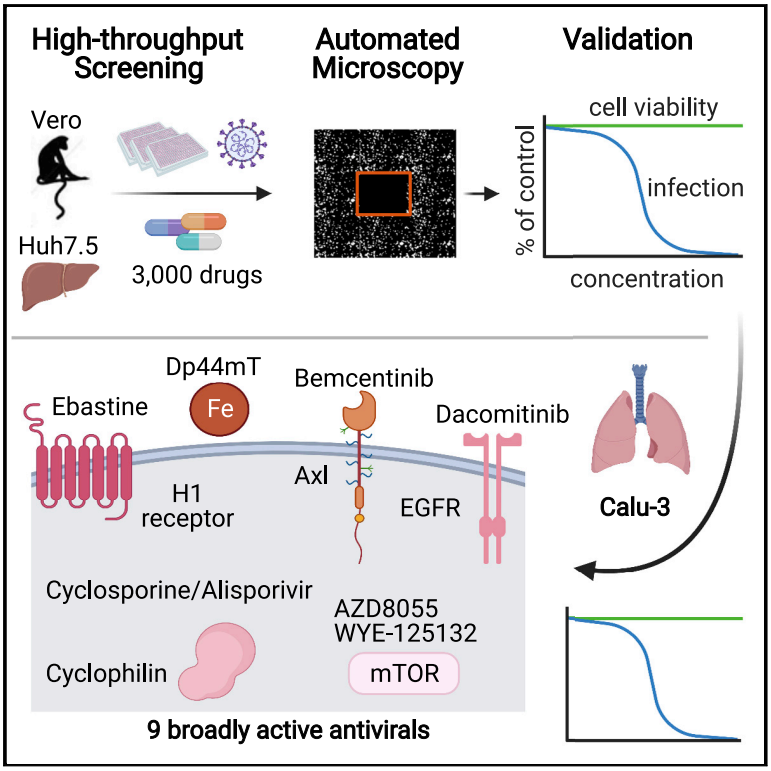
Exemple 1

Cell Reports

Resource

Drug repurposing screens reveal cell-type-specific entry pathways and FDA-approved drugs active against SARS-Cov-2

Graphical abstract



Highlights

- 3,000 compounds screened in two cell types against SARS-CoV-2
- Entry pathways are distinct in hepatocyte Huh7.5 and respiratory Calu-3 cells
- Only nine compounds that are active in Huh7.5 cells are active in Calu-3 cells
- Cyclosporin and cyclophilin inhibitors block SARS-CoV-2 infection in diverse cells

Authors

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In brief

There is an urgent need for antivirals to treat the newly emerged SARS-CoV-2. Dittmar et al. find nine host-directed drugs are antiviral in respiratory cells, seven of which have been given to humans, and three are FDA approved. We show host targets that have the potential for rapid clinical implementation.

Dittmar et al., 2021, Cell Reports *35*, 108959
April 6, 2021
https://doi.org/10.1016/j.celrep.2021.108959

CellPress

Cell Reports

CellPress
OPEN ACCESS

Resource

Drug repurposing screens reveal cell-type-specific entry pathways and FDA-approved drugs active against SARS-Cov-2

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SUMMARY

There is an urgent need for antivirals to treat the newly emerged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To identify new candidates, we screen a repurposing library of ~3,000 drugs. Screening in Vero cells finds few antivirals, while screening in human Huh7.5 cells validates 23 diverse antiviral drugs. Extending our studies to lung epithelial cells, we find that there are major differences in drug sensitivity and entry pathways used by SARS-CoV-2 in these cells. Entry in lung epithelial Calu-3 cells is pH independent and requires TMPRSS2, while entry in Vero and Huh7.5 cells requires low pH and triggering by acid-dependent endosomal proteases. Moreover, we find nine drugs are antiviral in respiratory cells, seven of which have been used in humans, and three are US Food and Drug Administration (FDA) approved, including cyclosporine. We find that the antiviral activity of cyclosporine is targeting Cyclophilin rather than calcineurin, revealing essential host targets that have the potential for rapid clinical implementation.

INTRODUCTION

Coronaviruses represent a large group of medically relevant viruses that were historically associated with the common cold. However, in recent years, members of the coronavirus family have emerged from animal reservoirs into humans and have caused novel diseases (Cui et al., 2019). First, severe acute respiratory syndrome coronavirus (SARS-CoV) emerged in China in 2003, followed by Middle East respiratory syndrome (MERS)-CoV in 2012 (de Wit et al., 2016; Weiss and Navas-Martin, 2005). Although SARS was in the end eradicated, MERS continues to cause infections in the Middle East. Beginning in December 2019 and continuing into January 2020, it became clear that a new respiratory virus was spreading in Wuhan, China. Rapid sequencing efforts revealed a coronavirus closely related to SARS, which was named SARS-CoV-2 (Wu et al., 2020). Unfortunately, this virus is highly infectious and has spread rapidly, creating a worldwide pandemic.

Identification of broadly acting SARS-CoV-2 antivirals is essential to clinically address SARS-CoV-2 infections. A potential route to candidate antivirals is through the deployment of drugs that show activity against related viruses. Previous studies found that the antiviral drug remdesivir, which was developed against the RNA-dependent RNA polymerase of Ebola virus, was also active against SARS-CoV-2 *in vitro*, with promising results in clinical trials (Beigel et al., 2020; Blanco-Melo et al., 2020; Warren et al., 2016). Chloroquine and its derivatives, including hydroxychloroquine, are approved for use in malaria, and many *in vitro* studies have found that these drugs are also active against coronaviruses, including SARS-CoV-2 (Liu et al., 2020; Wang et al., 2020). This led to early adoption of these agents to treat COVID-19 (the disease caused by SARS-CoV-2 infection); however, little efficacy of these agents has been demonstrated in subsequent clinical trials (Boulware et al., 2020). It remains unclear why these agents have not been more active in humans.

There are currently more than 3,000 US Food and Drug Administration (FDA)-approved drugs, as well as many others that have been tested in humans. We created an in-house library of 3,059 drugs, including ~1,000 FDA-approved drugs and ~2,100 drug-like molecules against defined molecular targets with validated pharmacological activity. In addition, we purchased drugs with reported anti-SARS-CoV-2 activity (e.g., remdesivir, lopinavir, azithromycin, etc.). Viruses encode unique proteins essential

Exemple 2

cmgh
CELLULAR AND MOLECULAR GASTROENTEROLOGY AND HEPATOLOGY

ORIGINAL RESEARCH

Drug Inhibition of SARS-CoV-2 Replication in Human Pluripotent Stem Cell–Derived Intestinal Organoids

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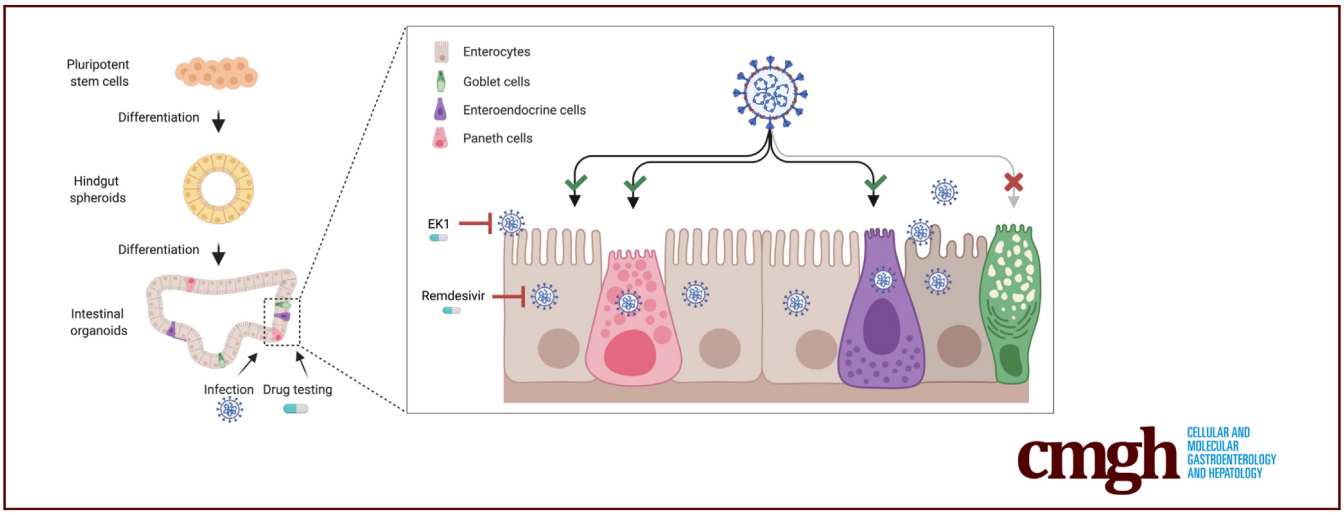

SUMMARY

Human pluripotent stem cell–derived intestinal organoids serve as an indefinite resource for organ-specific drug testing. SARS-CoV-2 infected and replicated within different cell types of the organoids, which was effectively inhibited by remdesivir and EK1 but not by famotidine.

BACKGROUND AND AIMS: The COVID-19 pandemic has spread worldwide and poses a severe health risk. While most patients present mild symptoms, descending pneumonia can lead to severe respiratory insufficiency. Up to 50% of patients show gastrointestinal symptoms like diarrhea or nausea, intriguingly associating with prolonged symptoms and increased severity. Thus, models to understand and validate drug efficiency in the gut of COVID-19 patients are of urgent need.

METHODS: Human intestinal organoids derived from pluripotent stem cells (PSC-HIOs) have led, due to their complexity in mimicking human intestinal architecture, to an unprecedented number of successful disease models including gastrointestinal infections. Here, we employed PSC-HIOs to dissect SARS-CoV-2 pathogenesis and its inhibition by remdesivir, one of the leading drugs investigated for treatment of COVID-19.

RESULTS: Immunostaining for viral entry receptor ACE2 and SARS-CoV-2 spike protein priming protease TMPRSS2 showed broad expression in the gastrointestinal tract with highest levels in the intestine, the latter faithfully recapitulated by PSC-HIOs. Organoids could be readily infected with SARS-CoV-2 followed by viral spread across entire PSC-HIOs, subsequently leading to organoid deterioration. However, SARS-CoV-2 spared goblet cells lacking ACE2 expression. Importantly, we challenged PSC-HIOs for drug testing capacity. Specifically, remdesivir effectively inhibited SARS-CoV-2 infection dose-dependently at low micromolar concentration and rescued PSC-HIO morphology.

CONCLUSIONS: Thus, PSC-HIOs are a valuable tool to study SARS-CoV-2 infection and to identify and validate drugs especially with potential action in the gut. *(Cell Mol Gastroenterol Hepatol 2021;11:935–948; https://doi.org/10.1016/j.jcmgh.2020.11.003)*

Keywords: SARS-CoV-2; COVID-19; Intestinal Organoids; Remdesivir; Famotidine.

Exemple 3

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Season-dependent effects of ZnO nanoparticles and elevated temperature on bioenergetics of the blue mussel *Mytilus edulis*

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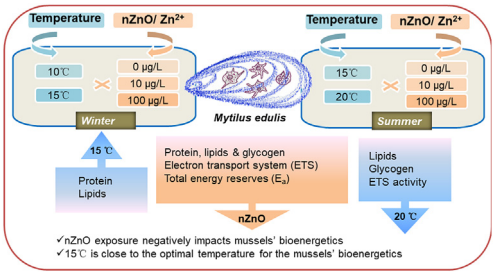
HIGHLIGHTS

- Combined effects of temperature and nZnO on mussels' bioenergetics were studied.
- In summer and winter, nZnO exposure depleted glycogen stores of the mussels.
- In summer, nZnO exposure suppressed mitochondrial activity and lipid levels.
- Warming (+5 °C) increased mussels' energy reserves in winter but not in summer.

GRAPHICAL ABSTRACT



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ABSTRACT

Input of ZnO nanoparticles (nZnO) from multiple sources have raised concerns about the potential toxic effects on estuarine and coastal organisms. The toxicity of nZnO and its interaction with common abiotic stressors (such as elevated temperature) are not well understood in these organisms. Here, we examined the bioenergetics responses of the blue mussel *Mytilus edulis* exposed for 21 days to different concentrations of nZnO or dissolved zinc (Zn^{2+}) **(0, 10, 100 μg l^{-1})** and two temperatures (ambient and 5 °C warmer) in winter and summer. Exposure to nZnO had little effect on the protein and lipid levels, but led to a significant depletion of carbohydrates and a decrease in the electron transport system (ETS) activity. Qualitatively similar but weaker effects were found for dissolved Zn. In winter mussels, elevated temperature (15 °C) led to elevated protein and lipid levels increasing the total energy content of the tissues. In contrast, elevated temperature (20 °C) resulted in a decrease in the lipid and carbohydrate levels and suppressed ETS in summer mussels. These data indicate that moderate warming in winter (but not in summer) might partially compensate for the bioenergetics stress caused by nZnO toxicity in *M. edulis* from temperate areas such as the Baltic Sea.

1. Introduction

With the global rise in nanotechnology, manufactured

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