

Un nouveau membre a rejoint le réseau GABRIEL en fin d'année : le Centre d'Infectiologie Charles Mérieux / Laboratoire Rodolphe Mérieux de Rio Branco, Brazil

Cette institution permet ainsi de renforcer la présence et les activités de recherche du réseau GABRIEL en Amérique du Sud, notamment dans la région d'Amazonie.

Plus d'informations sur ce nouvel arrivant dans l'article ci-dessous.



Le CICM/LRM (Centro de Infectiologia Charles Mérieux / Laboratório Rodolphe Mérieux) est un laboratoire de biosécurité de niveau 2 et 3, situé au sein de l'hôpital de l'État d'Acre (FUNDHACRE) au Brésil. Il a récemment rejoint le réseau GABRIEL, renforçant ainsi l'engagement régional en faveur de la recherche, du diagnostic moléculaire et de la formation sur les maladies infectieuses tropicales.

Sa mission consiste à déployer des outils de diagnostic et à établir des programmes de surveillance des pathogènes émergents et résistants dans la région amazonienne et dans l'environnement hospitalier, tels que les bactéries et les champignons de type levure. Elle consiste également à surveiller la multirésistance aux médicaments dans la

Sommaire

- *Un nouveau membre a rejoint le réseau GABRIEL en fin d'année*
- *Consortium Brésil, Cameroun et Madagascar : réflexion sur la propagation de la résistance aux antimicrobiens et aux biocides des eaux usées vers l'environnement*
- *Étude de la transmission de la résistance aux antimicrobiens*
- *Caractéristiques des patients COVID-19 hospitalisés à l'admission et facteurs associés à la gravité clinique dans les pays à faible et moyen revenus : une étude d'observationnelle*
- *Aborder la problématique du diagnostic de la tuberculose chez l'enfant*
- *INSEQBIN : Nouveau cours en ligne sur le Séquençage Nouvelle Génération et la Bio-informatique !*
- *Publications des membres du réseau GABRIEL 2023-2024*

tuberculose et à diagnostiquer les virus respiratoires et les arbovirus (tels que la dengue). Le laboratoire a mené des études avancées sur l'hépatite chronique (HDV).

Le laboratoire se consacre également à la formation continue et à l'amélioration des compétences des professionnels de santé, en se concentrant sur les maladies infectieuses et en investissant dans les jeunes chercheurs.



Ces activités sont menées en partenariat avec Fiocruz Porto Velho, qui offre son expertise sur les questions de santé publique régionales, renforçant ainsi les capacités scientifiques et de laboratoire.

Une autre priorité est d'améliorer les stratégies et les efforts visant à collecter des ressources financières pour mener à bien ces activités. L'établissement de partenariats internationaux (y compris avec les partenaires du réseau GABRIEL) apporte des ressources et de la visibilité au laboratoire. Au niveau national, il existe déjà des collaborations efficaces avec des universités publiques, des centres de recherche et des fondations de soutien à la recherche.

En résumé, le CICM/LRM est conforme

aux directives de diagnostic du ministère brésilien de la Santé en ce qui concerne les maladies infectieuses.

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Consortium Brésil, Cameroun et Madagascar : réflexion sur la propagation de la résistance aux antimicrobiens et aux biocides des eaux usées vers l'environnement

La pandémie de COVID-19 est apparue au cours d'une période où la résistance aux antimicrobiens (RAM), défi majeur pour la santé mondiale, générait beaucoup d'inquiétudes. Les mesures d'hygiène visant à prévenir la pandémie de COVID-19, associées à l'utilisation d'antimicrobiens, peuvent avoir un impact sur l'évolution de la résistance aux antimicrobiens. Les antimicrobiens et les biocides utilisés dans les hôpitaux et les collectivités pénètrent dans les stations d'épuration des eaux usées (STEU) et peuvent se retrouver dans les systèmes naturels, entraînant la pollution des écosystèmes aquatiques par des résidus et des bactéries résistantes aux antimicrobiens (ARB). Cela accroît la propagation de la RAM et provoque des risques indirects pour la santé humaine et animale.

Dans les pays à revenu faible ou intermédiaire comme le Cameroun et Madagascar, les eaux usées non traitées sont souvent déversées directement dans les rivières et les ruisseaux en raison du non-fonctionnement des stations d'épuration. Au Brésil, les STEU existantes n'éliminent

pas complètement les antimicrobiens et les biocides, ce qui contribue à la propagation de la RAM dans les eaux de surface. Ces masses d'eau contaminées sont utilisées pour les activités de loisirs et l'irrigation, augmentant encore cette propagation. Dans les bidonvilles, l'absence de STEU entraîne une contamination directe des masses d'eau, ce qui aggrave le problème.

Les études sur la propagation de la RAM dans l'environnement, en particulier en Europe, en Asie et aux États-Unis, se sont principalement concentrées sur la caractérisation de la résistance dans des sites spécifiques, en tenant compte de la pression de sélection exercée par les antimicrobiens présents dans l'environnement. L'impact de la COVID-19 sur la persistance et la propagation de l'ARB n'est pas encore documenté.



Le consortium COV-AMR (Cameroun, Madagascar et Brésil) vise à évaluer l'impact de la pandémie de COVID-19 sur la propagation de la résistance aux antimicrobiens et aux biocides dans l'environnement. De janvier à juin 2022, des prélèvements mensuels d'eau ont été effectués dans des établissements de santé traitant des patients atteints de COVID-19 et dans des sites de contrôle afin de rechercher des bactéries multirésistantes, d'analyser les déterminants de la résistance et d'identifier les caractéristiques génétiques à l'aide du séquençage du génome entier. Les résidus

d'antimicrobiens et de biocides ont été quantifiés par chromatographie liquide et spectrométrie de masse. Le microbiome de l'eau a été analysé à l'aide de la plateforme Ion Torrent et de l'outil QIIME2. La présence du SARS-CoV-2 a été étudiée par RT-qPCR.

L'étude a montré que pendant la pandémie de COVID-19, les effluents des hôpitaux et des zones urbaines au Cameroun, au Brésil et à Madagascar ont facilité la propagation de la RAM et de la résistance aux biocides dans l'environnement. Cette exposition risque d'entraîner l'acquisition de gènes de résistance par les bactéries indigènes et de confronter les populations à des infections difficiles à traiter. Les autorités doivent s'assurer que les stations d'épuration fonctionnent de manière à éliminer la flore microbienne et à neutraliser les résidus d'antimicrobiens. Les populations qui utilisent de l'eau contaminée doivent observer une hygiène stricte. Les gouvernements doivent appliquer les réglementations relatives à la gestion des eaux usées hospitalières et municipales, avec des évaluations et des rapports périodiques sur les résidus d'antimicrobiens et les déterminants de la résistance.

Les résultats de l'étude permettront de sensibiliser le public à la contamination aux résidus d'antimicrobiens et à la résistance aux antimicrobiens, et d'alerter sur la nécessité de protéger l'environnement et la santé.

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Étude de la transmission de la résistance aux antimicrobiens



Les femmes enceintes, compte-tenu de leur immunité affaiblie, sont particulièrement susceptibles aux infections bactériennes. Le portage de BLSE pendant la grossesse peut entraîner des infections urinaires potentiellement mortelles, pouvant affecter les nouveau-nés en raison de la transmission fécale-vaginale (Denkel et al., 2014 ; Bulabula et al., 2017). Notre étude collaborative avec les pays du réseau GABRIEL—le Bangladesh, le Paraguay et le Brésil—vise à déterminer la prévalence d'*E. coli* BLSE parmi les mères enceintes en bonne santé dans les zones urbaines,

tout en explorant l'impact potentiel des animaux de compagnie sur la transmission des BLSE. Au Bangladesh, l'Institut pour le développement des initiatives en sciences et santé (ideSHi) a obtenu l'approbation du comité d'éthique (IRB) pour cette étude le 25 avril 2023 et a débuté le recrutement des participants à partir du 1er mai 2023.

Les données préliminaires du Bangladesh indiquent un taux de portage de BLSE de 85 % parmi les femmes enceintes sans animaux de compagnie, et de 92 % en présence d'animaux. De plus, 60 % des animaux de compagnie sont porteurs de *E. coli* BLSE. Cette forte prévalence de portage d'ESBL, indépendamment de la présence d'animaux de compagnie, est unique au Bangladesh par rapport aux autres pays collaborateurs. Ces résultats peuvent expliquer pourquoi des taux élevés d'infections bactériennes pouvant être une menace pour la santé, sont observés dans certains contextes des pays à revenu faible et intermédiaire comme le Bangladesh, et indiquent la présence d'une augmentation des bactéries résistantes à l'échelle mondiale.

Au-delà des observations phénotypiques, l'étude vise à réaliser le séquençage du génome entier de 100 isolats afin d'étudier les types de souches parmi les échantillons appariés humains et animaux, ainsi que les changements des sérotypes d'*E. coli* parmi les individus au cours du temps. ideSHi utilisera sa plateforme génomique (Illumina MiSeq) pour le séquençage. Le soutien en réactifs du réseau GABRIEL permet de poursuivre cette recherche et de générer des données génomiques à haut débit afin de mieux comprendre la situation.

Les résultats de l'étude devraient mettre en évidence le lien entre les animaux de compagnie et les humains en ce qui concerne la circulation des BLSE et permettre de mieux comprendre les raisons d'un portage élevé dans le microbiote intestinal humain, en particulier au Bangladesh, qui peut être influencé par divers facteurs, indépendamment de la présence des animaux de compagnie.

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Caractéristiques des patients COVID-19 hospitalisés à l'admission et facteurs associés à la gravité clinique dans les pays à faible et moyen revenus : une étude d'observationnelle

Le virus du SARS-CoV-2, apparu en décembre 2019 à Wuhan, en Chine, s'est rapidement propagé dans le monde entier. Au 10 mars 2023, on comptait 676 609 955 cas confirmés de COVID-19 et 6 881 955 décès dans le monde. Bien que l'OMS ait déclaré la fin de l'urgence mondiale COVID-19 le 5 mai 2023, le virus continue de circuler malgré les efforts de vaccination généralisés.

Le profil du COVID-19, y compris les symptômes, la guérison et les taux de mortalité, est influencé par le triangle épidémiologique : l'agent pathogène, l'hôte et l'environnement. Les facteurs liés à l'hôte, tels que l'âge avancé et les comorbidités sous-jacentes, sont des facteurs de risque

indépendants pour la gravité et la mortalité du COVID-19. Dans les pays à revenu faible et intermédiaire (PRFI), comme ceux d'Afrique de l'Ouest et d'Asie du Sud, la population est essentiellement composée de jeunes adultes, ce qui laisse présager une maladie potentiellement moins grave et des taux de mortalité plus faibles. Cependant, la forte prévalence de comorbidités chez les jeunes adultes des PRFM peut augmenter le risque de maladie grave. En outre, les habitations surpeuplées, la co-circulation de plusieurs agents infectieux et les systèmes de santé plus fragiles ne disposant pas d'unités de soins adaptés pourraient avoir un impact sur les conséquences de la maladie dans les PRFM.

Malgré des recherches approfondies sur le COVID-19 dans les pays à revenu élevé, peu d'éléments sont connus sur les caractéristiques cliniques et le devenir des patients dans les PRFM. Cette étude visait à décrire les caractéristiques cliniques de patients atteints de COVID-19 et hospitalisés dans six PFRM au cours de la première année de la pandémie. L'étude observationnelle, prospective et multicentrique en milieu hospitalier a inclus des participants du Bangladesh, de la Guinée, de la Côte d'Ivoire, du Liban, de Madagascar et du Mali, du 5 mars 2020 au 4 mai 2021.

L'étude a analysé la gravité clinique du COVID-19, définie comme l'admission en unité de soins intensifs (USI) ou le décès, en utilisant des modèles de régression logistique multivariés pour identifier les variables indépendantes associées à la gravité de la maladie. Au total, 1 096 patients ont été inclus, avec un âge médian de 49 ans, allant

de 38 ans au Mali à 63 ans en Guinée. La gravité clinique globale du COVID-19 était de 12,3 %, variant de 6,4 % au Mali à 18,8 % en Guinée. Les maladies cardiovasculaires étaient indépendamment associées à la gravité clinique dans les deux groupes d'âge (<60 et ≥60 ans), tandis que le diabète était également un facteur significatif chez les patients de moins de 60 ans.

L'étude conclut que la gravité du COVID-19 et la mortalité dans les PRFM sont principalement dues à l'âge, mais que les maladies chroniques augmentent considérablement le risque de gravité, en particulier chez les patients plus jeunes.

Cette étude a été récemment publiée dans l'American Journal of Tropical Medicine and Hygiene : <https://www.ajtmh.org/view/journals/tpmd/aop/article-10.4269-ajtmh.23-0456/article-10.4269-ajtmh.23-0456.xml>.

Nous tenons à remercier toutes les personnes impliquées dans l'étude pour leur soutien dans la réalisation de ce travail essentiel pendant la période difficile du COVID-19, et nous nous réjouissons des futures collaborations. Tous les coauteurs sont cités par ordre alphabétique.

Marianne Abifadel, Kaousar Ahmed, Sayera Banu, Ibrahima Camara, Fahmida Chowdhury, Daouda Coulibaly, Georges Dabar, Cedric Dananché, Rachel Daw, Zakiul Hassan, Magali Hervé, Ariful Islam, Florence Komurian-Pradel, Jean-Pierre Kouamé, Bourema Kouriba, Josette Najjar-Pellet, Andoniaina Rakotonaivo, Felana Ranaivo-Rabetokotany, Mandranto Rasamoelina, Tiavina Rasoloforison, Moussa Riachi, Mitra Saadatian-Elahi, Luc Samison, Valentina Sanchez Picot, Sita Savané, Ismaila Thera,

Abdoulaye Touré, and Philippe Vanhems

Aborder la problématique du diagnostic de la tuberculose chez l'enfant



Le diagnostic et la gestion de la tuberculose (TB) chez les enfants de moins de 10 ans représentent un problème de santé publique majeur à l'échelle mondiale, et sont une priorité pour l'OMS¹. En 2022, on estime que 1,25 million d'enfants et de jeunes adolescents (0-14 ans) ont contracté la TB, mais que 51 % d'entre eux ne sont pas diagnostiqués et déclarés². **Il est urgent de développer des tests rapides, précis et moins invasifs qui ne reposent pas sur les expectorations pour le triage et la confirmation de la TB infantile.**

Plusieurs activités et initiatives sont en cours au sein du réseau GABRIEL pour contribuer à cet objectif global :

Évaluation de l'utilisation des selles avec Xpert Ultra comme outil de diagnostic pour la TB chez les enfants : icddr,b au Bangladesh travaille depuis longtemps sur cette approche³. Tester les selles avec Xpert-Ultra offre une méthode plus efficace pour diagnostiquer la TB pulmonaire infantile. Cependant, la positivité varie

selon les symptômes/critères présentés, ce qui suggère la nécessité d'une évaluation soigneusement conçue du parcours diagnostique pour assurer une utilisation optimale des ressources diagnostiques limitées. L'équipe de Dr. Sayera Banu publiera bientôt les résultats et partagera son expérience sur le déploiement à l'échelle nationale de cette approche.

Évaluation de RISK6 comme un outil de diagnostic pour la TB infantile : RISK6 est un test sanguin non basé sur l'expectoration qui a été évalué en 2021 au sein du réseau GABRIEL pour le diagnostic de la TB chez l'adulte⁴. Il est actuellement évalué comme test de triage pour la TB chez les enfants au Bangladesh (étude DEDICATE⁵).

Recherche opérationnelle visant à améliorer le diagnostic de la TB infantile : En accord avec la dernière feuille de route de l'OMS pour mettre fin à la TB chez les enfants et les adolescents, la Fondation Mérieux, en collaboration avec l'Institut national de recherche biomédicale et l'organisation à but non lucratif « One Health Conservation Initiative » (**République démocratique du Congo**), l'Institut Pasteur de Madagascar (**Madagascar**) et l'Institut Pasteur du Cambodge (**Cambodge**), a co-développé le protocole de recherche opérationnelle IDTB4Child. Ce protocole vise à améliorer le diagnostic de la TB infantile grâce à la mise en œuvre, l'évaluation des performances et du rapport coût-efficacité des Algorithmes de Décision de Traitement (ADT), du nouveau test rapide RISK6 réalisé à partir d'une goutte de sang prélevé au bout du doigt, et d'autres approches innovantes telles que les tests respiratoires⁶ et la **radiographie numérique**

assistée par ordinateur⁷, pour améliorer la détection de la TB chez les enfants et leurs contacts familiaux.

Les stratégies innovantes et les nouvelles approches pour la prévention et le diagnostic de la TB infantile développées par plusieurs membres du réseau GABRIEL devraient être mises en lumière cette année à travers une série de publications dans l'**International Journal of Tuberculosis and Lung Disease** (IJLD). Une session sur cette thématique sera également animée lors de la réunion du réseau GABRIEL (27-29 novembre 2024), afin de partager les expériences et d'explorer de nouvelles opportunités de partenariats et de financements pour des projets de recherche opérationnelle à mettre en œuvre au sein du réseau.

¹WHO. Global tuberculosis report 2023. <https://www.who.int/publications-detail-redirect/9789240083851>.

²WHO | Roadmap towards ending TB in children and adolescents. WHO <http://www.who.int/tb/publications/2018/tb-childhoodroadmap/en/>.

³Kabir, S. et al. Xpert Ultra Assay on Stool to Diagnose Pulmonary Tuberculosis in Children. Clin Infect Dis 73, 226–234 (2021).

⁴Bayaa, R. et al. Multi-country evaluation of RISK6, a 6-gene blood transcriptomic signature, for tuberculosis diagnosis and treatment monitoring. Sci Rep 11, 13646 (2021).

⁵DEDICATE (blooD-basEd DiagnosiC of pAucibacillary Tb in bangladEsh). Mérieux Foundation <https://www.fondation-merieux.org/en/projects/dedicate-blood-based-diagnostic-of-paucibacillary-tb-in-bangladesh/> (2013).

⁶EBC-LAM. Mérieux Foundation <https://www.merieux-lam.com>

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⁷Kaguje, M. et al. The Performance of Computer-Aided Detection Digital Chest X-ray Reading Technologies for Triage of Active Tuberculosis Among Persons With a History of Previous Tuberculosis. Clinical Infectious Diseases 76, e894–e901 (2023).

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INSEQBIN : Nouveau cours en ligne sur le Séquençage Nouvelle Génération et la Bio-informatique !



La bio-informatique joue un rôle essentiel dans l'analyse des données biologiques. En combinant la biologie et l'informatique, elle permet d'extraire et d'analyser les informations génétiques, ouvrant la voie à des avancées significatives dans des domaines variés. Ses applications dans la génomique sont particulièrement importantes, notamment pour l'étude de l'évolution, la médecine personnalisée, la découverte de nouveaux biomarqueurs ou la surveillance d'agents pathogènes.

C'est pourquoi nous sommes ravis de vous annoncer le lancement de notre nouveau cours en ligne, «Introduction au Séquençage Nouvelle Génération et à la Bio-informatique»

Septembre 2024 | Numéro 33
(INSEQBIN), développé en partenariat avec FIND et la Fondation Mérieux. Disponible à partir du 15 septembre 2024 en français et en anglais, ce cours propose six modules présentant les technologies de séquençage Illumina et Oxford Nanopore, ainsi que les étapes clés d'analyse bio-informatique à savoir l'évaluation de la qualité et le nettoyage des données brutes, l'assemblage de séquences, l'annotation des résultats, ainsi que l'alignement de séquences et l'identification de variations génétiques.

Ce cours s'adresse aux étudiants, aux techniciens de laboratoire et aux chercheurs en biologie, génétique ou médecine, impliqués dans des projets de séquençage et souhaitant développer leurs connaissances en bio-informatique.

Pour plus d'informations et pour vous inscrire, veuillez consulter notre page dédiée: <https://www.fondation-merieux.org/evenements/inseqbin-nouveau-cours-en-ligne-sur-la-bio-informatique/>

Emilie Westeel, Fondation Mérieux

Publications des membres du réseau GABRIEL 2023-2024

Publications collaboratives

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Le réseau GABRIEL bénéficie du soutien de bioMérieux

