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► To cite this version:

Lucie Sauzéat, Emilien Bernard, Armand Perret-Liaudet, Isabelle Quadrio, Alain Vighetto, et al.. Interdisciplinary Case Study: Geochemistry Meets the Clinic in Search for a Metal ALS Biomarker. *iScience*, 2019, 11, pp.531-535. 10.1016/j.isci.2018.12.007 . hal-02323839

HAL Id: hal-02323839

<https://hal.science/hal-02323839>

Submitted on 17 Mar 2022

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Pascal Leblanc and Vincent Balter Sitting In Front of a Isotope Mass Spectrometer at the ENS de Lyon

Backstory

Interdisciplinary Case Study: Geochemistry Meets the Clinic in Search for a Metal ALS Biomarker

Lucie Sauzéat, Emilien Bernard, Armand Perret-Liaudet, Isabelle Quadrio, Alain Vighetto, Pierre Krolak-Salmon, Emmanuel Broussolle, Pascal Leblanc, and Vincent Balter

Human neurons require trace amounts of a dozen or so metals to function. An excess or deficit of these essential metals can disrupt cellular activity, and such imbalances are associated with a long list of brain disorders, including neurodegeneration. That is why Vincent Balter, a geochemist at the Université de Lyon and CNRS, and Pascal Leblanc, a neurobiologist at the Institut NeuroMyoGéne, joined their laboratories with clinicians at Hospices Civils de Lyon to identify specific metal irregularities in patients with amyotrophic lateral sclerosis (ALS). Their project linked a specific copper isotope composition in the cerebrospinal fluid to ALS, helping to unravel some of the molecular mechanisms at work in the disease and bringing forth a new candidate biomarker.

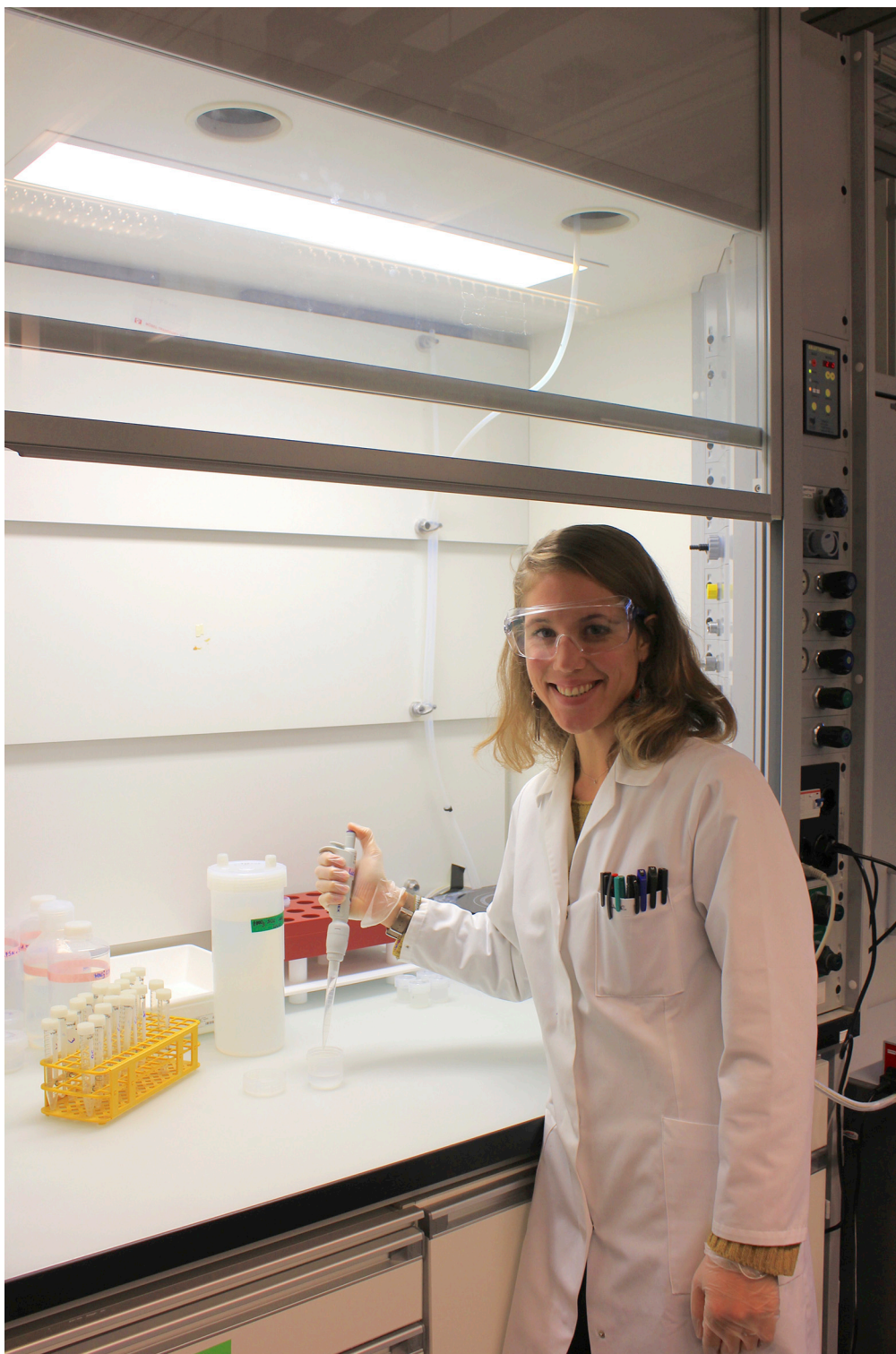
This is what brought everyone together for "Isotopic Evidence for Disrupted Copper Metabolism in Amyotrophic Lateral Sclerosis," published on August 1 in *iScience* ([https://www.cell.com/iscience/fulltext/S2589-0042\(18\)30111-1](https://www.cell.com/iscience/fulltext/S2589-0042(18)30111-1)).

PROXIMITY

Geography Does Not Guarantee Collaboration, Respect Does

Historically, clinicians and biologists studying neurodegenerative diseases were close to each other for obvious scientific reasons. The link with geochemistry is that biologists and geochemists are both based at the Ecole Normale Supérieure de Lyon and had a previous interdisciplinary success. That said, we all had other experiences with colleagues from the same hospital or the same academic institution, which





Lucie Sauzéat Preparing the Samples in a Clean Room for Isotopic Measurements

were not successful. Why? Because the main criterion for a fruitful collaboration is respect. People must be respectful to others' disciplines and must be convinced that their own discipline has some limits that can be pushed forward only with external input.



Isabelle Quadrio and Armand Perret-Liaudet in the Laboratory of Neurobiology of Hospices Civils de Lyon

LANGUAGE

Take Time to Avoid Jargon

Language gaps will be filled relatively easily if teammates are both attentive and avoid speaking in jargon. Part of being respectful to others is taking time to explain things in layman terms (which means that all collaborators perfectly understand what the others are talking about). Regular meetings are important, but visiting other laboratories is essential. Of course, curiosity helps.

RESEARCH METHODS

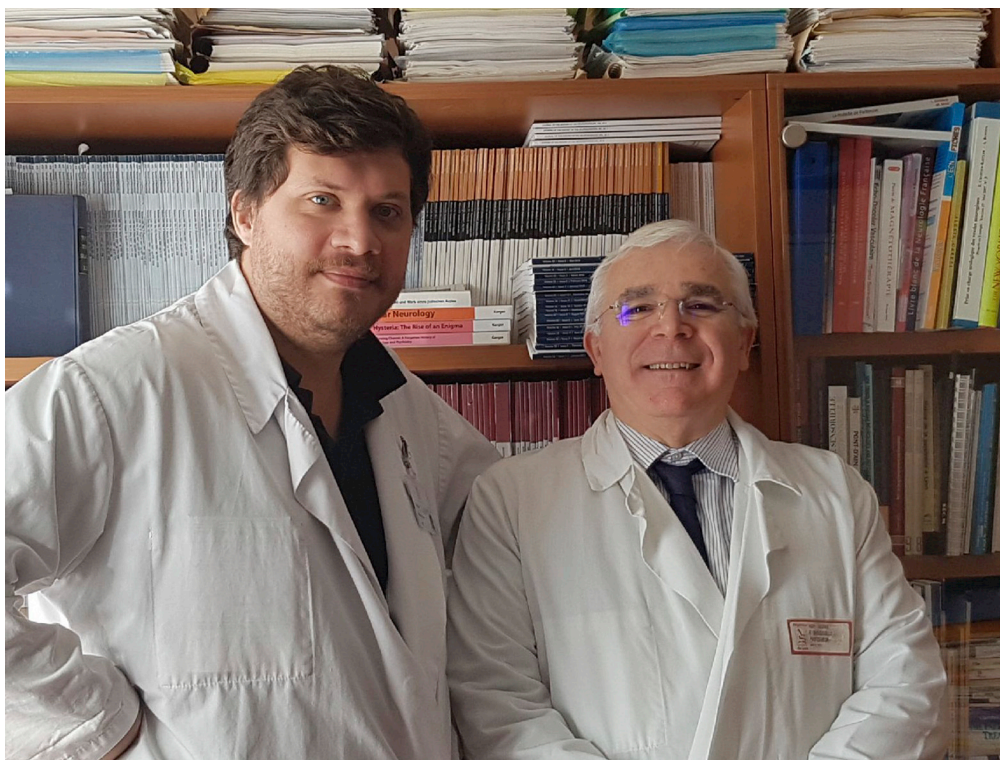
Work through Technical Challenges Early

Once a common goal is clearly defined (which can be considered the first milestone), tailoring experiments according to all constraints, being analytical (e.g., sample size, storage conditions, blanks), sanitary (e.g., treatment of infectious samples), and administrative (e.g., various authorizations), is crucial. Most of the time, translational research ends up stalling due to a technical problem that was not correctly identified in the first place.

In our case, we took great care with the handling of human cerebrospinal fluid samples because initial metal levels are very low and could have been easily contaminated. So, before studying real samples, we analyzed metal blank levels in all the plastic materials that are routinely used for the sampling and storage of cerebrospinal fluids. We then checked that matrix effects were minimal during the chromatographic extraction of metals. During this “dead time,” clinicians validated all the necessary authorizations to the review boards of the hospitals. Everybody was on the starting blocks when the time arrived to analyze real samples (which can be considered as a second milestone).

The main criterion for a fruitful collaboration is respect. People must be respectful to others' disciplines and must be convinced that their own discipline has some limits that can be pushed forward only with external input.

Tailoring experiments according to all constraints, analytical, sanitary, and administrative, is crucial. Most of the time, translational research ends up stalling due to a technical problem that was not correctly identified in the first place.



Emilien Bernard and Emmanuel Broussolle in the Neurology Hospital of Hospices Civils de Lyon

PUBLICATION

Finding a Home for Atomic Biology

Publication is the third milestone. The nature of the project itself should determine the journal, but it is not that simple. In our case, publishing the results in a journal dedicated to neurological diseases that is read only by clinicians who do not have a background on stable isotope fractionation or a relationship with their local geology laboratory would have been a pity. The final goal of course is to publish in the best journal of neurology, but we still have a long road ahead, so an interdisciplinary journal that accepts papers on atomic biology—a new area wherein classical journals are not venturing—was the best option.

Discussions regarding the position of the authors can be tricky because interdisciplinarity means at least two teams, sometimes more, wherein all claim for a single first and last position in the author list. Perhaps a possible solution would be to propose unlimited co-first and co-last positions in the author list.

GOVERNANCE

Career Rewards and Risks with Interdisciplinary Work

Our team has diverse jobs and positions, and so the members have different perspectives on the professional implications for doing interdisciplinary work. For Lucie Sauzéat, who is the first author and was a PhD student in geochemistry, having an experience that straddled multiple fields showed that she could adjust her experience to different problems, which has been a good talking point when looking for a job.

When Vincent Balter moved forward with biomedical applications of stable isotope geochemistry almost 10 years ago, it had all the excitement of discovering a new continent. “You have a permanent position at the CNRS, so you have to take risks, otherwise who will?” a geologist friend asked at the time. That said, having a promotion with an interdisciplinary profile is tricky because evaluation panels are generally composed according to disciplines, and downgrading a candidate just because she or he does not entirely fit the discipline’s perimeter is an easy way to reach a shortlist.

Funding of interdisciplinary research is hard because some purely disciplinary mechanisms of selection, like those at work for professional promotion, can lead to unsuccessful proposals. Hopefully, we have in France the Mission pour les Initiatives Transverses et l'Interdisciplinarité at the CNRS, one of the objectives of which is to help and fund interdisciplinary researches. Moreover, starting collaborations with no proof of concept also rarely receives grants. Interdisciplinary papers are also often "Sleeping Beauties," meaning that they will begin to be cited a long time after the publication date.

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Final Thoughts

In summary, interdisciplinary/translational research implies respect of other people involved in the project, a lot of discussions until each person understands what the others are doing, and the elaboration of a simple and common objective and the respective role of each person to reach it (in the meantime, try to avoid stowaway passengers).

The interdisciplinary case study series highlights how research teams have overcome the barriers related to proximity, language, methods, governance, publication, and funding that arise when bringing people together from two or more unrelated fields. Read more backstories and get inspired at *iScience*.