The Birchal Centre, Keele University and Centro de Investigación Científica de Yucatán

THE THIRTEENTH KEELE MEETING ON Aluminium

Future Challenges in the Aluminium Age

23rd 27th March 2019

Hotel Uxmal Resort Maya
Yucatán, México

Keele University
CONACYT
CICY
SCIENTIFIC PROGRAMME

Saturday 23rd March 2019

17.00 Registration and Poster Assembly
19.30 Welcome to Meeting / Welcome Buffet

Traditional Music and Dance from the Yucatán

Sunday 24th March 2019

The Conference is Open!

Session 1

Aluminium and the Environment

*Denotes presentation by a student.

Chair: Charley Driscoll (Syracuse University, New York, USA)

08.55 Introduction by the Chair
9.00 Platform 1
Silicic acid
Chris Exley (Keele University, United Kingdom)

9.20 Discussion

9.30 Platform 2
Interaction of aluminum and silica with anaerobic acidophiles: A geochemical perspective with emphasis on biomineralization
Javier Sánchez-España (Spanish Geological Survey, Spain)

9.50 Discussion
10.00 Platform 3
New evidence for the iron-aluminum hypothesis (Al could play an important role in the ocean carbon cycle and climate change)
Linbin Zhou (South China Sea Institute of Oceanology, China)

10.20 Discussion

10.30 COFFEE

10.50 Platform 4
The influence of soil vegetation cover and precipitation on soil aluminium pools
Petra Vokurková (Czech University of Life Sciences, Prague, Czech)

11.10 Discussion

11.20 Platform 5*
Changes in low molecular weight organic acid production as indicators of fungal response to aluminium stress
Filip Polák (Comenius University in Bratislava, Slovakia)

11.40 Discussion

11.50 Oral Poster 1*
Effect of aluminum on the growth, sporulation and virulence of Pythium ultimum
Normig Zoghbi-Rodríguez (CICY, México)

11.55 Discussion

12.00 Platform 6*
Aluminum exposure in honey bees: effects on forage, lifespan, and the cholinergic system
Ana Chicas-Mosier (Oklahoma State University, USA)

12.20 Discussion

12.30 Platform 7
The effect of river water acidity and aluminium on boreal fish assemblages and fish kills
Tapio Sutela (Natural Resources Institute, Finland)

12.50 Discussion

13.00 LUNCH
Session 2

Aluminium and Plants

*Denotes presentation by a student.

Chair: Ondřej Drábek (Czech University of Life Sciences Prague, Czech)

14.25  Introduction by the Chair

14.30  Platform 8
Foliar aluminum concentration of Central America tree species
Alfredo Alvarado-Hernández (University of Costa Rica, San José, Costa Rica)

14.50  Discussion

15.00  Platform 9
Aluminium and phosphorus availability to tea plants (Camellia sinensis)
influences leaf polyphenol patterns
Charlotte Poschenrieder (Universidad Autónoma de Barcelona, Spain)

15.20  Discussion

15.30  Oral Poster 2*
Elucidating aluminum accumulation in plants by mapping techniques
Angela Ku-González (CICY, México)

15.35  Discussion

15.40  Platform 10
Studies on Al-tolerance mechanisms in seedlings of Fagopyrum esculentum
Moench
Rocío Cruz-Ortega (Institute of Ecology, UNAM, México)

16.10  Oral Poster 3*
Wild rice Oryza glumaepatula as a new source of aluminum tolerance genes for
improving yields of cultivated Oryza sativa in acid soils
Juan Montoya-Díaz (Icesi University, Cali, Colombia)

16.15  Discussion

16.20  TEA
16.50  Platform 11
**Study of aluminium toxicity effect on secondary metabolites production and signal transduction mechanisms in two suspension cells cultures**
Tere Hernández-Sotomayor (*CICY, México*)

17.10  Discussion

17.20  Oral Poster 4*
**Aluminum modifies the protein binding of different molecular species of phosphatidic acid in suspension cells of Coffea arabica L.**
Roberto Pech-Kú (*CICY, México*)

17.25  Discussion

17.30  Platform 12*
**Effect of the nitrogen source on aluminium toxicity in suspensions cells of Coffea arabica L.**
Jacqueline Cerdas-Solano (*University of Costa Rica, Guanacaste, Costa Rica*)

17.50  Discussion

18.00  Oral Poster 5*
**Nitrate reductase-dependent nitric oxide production is involved in the response to aluminum stress in Coffea arabica L. suspension cells**
Laura Esquivel-Hernández (*CICY, México*)

18.05  Discussion

18.10  Oral Poster 6*
**Role of salicylic acid induced phenylpropanoids in response to aluminum stress in Capsicum chinense cell cultures**
Ibis Vargas-Paredes (*CICY, México*)

18.15  Discussion

18.20  **END OF FIRST DAY**

20.15  **DINNER**

21.15  **Social Event including official Poster Session and Tequila Tasting!**
Monday 25th March 2019

Session 3

Human Exposure to Aluminium

*Denotes presentation by a student.

Chair: Tere Hernández-Sotomayor (CICY, México)

08.25 Introduction by the Chair

08.30 Platform 13
Computational approach to aluminum biochemistry: How aluminum can alter the thermodynamics of redox reactions
Xabier Lopez (University of San Sebastian, Donostia, Euskadi, Spain)

08.50 Discussion

09.00 Platform 14
Speciation analysis of aluminium organic complexes, method development and application in food analysis
Marcin Frankowski (Adam Mickiewicz University, Poznań, Poland)

09.20 Discussion

09.30 Platform 15
Aluminium chloride triggers neuroinflammation in vitro on microglial cells: possible involvement of the purinergic system
Maria Rosa Chitolina (Federal University of Santa Maria, RS, Brazil)

09.50 Discussion

10.00 Oral Poster 7*
Role of LncRNA BACE1-AS on regulating Aβ in neuronal injury induced by aluminum exposure
Bao-long Pan (Shanxi Medical University, Taiyuan, China)

10.05 Discussion

10.10 COFFEE
10.30  Platform 16
**Effect of MLL modified H3K4me3 on aluminum induced cognitive impairment—Both population and animal epigenetic studies**
Qiao Niu (Shanxi Medical University, Taiyuan, China)

10.50  Discussion

11.00  Oral Poster 8*
**Role of mGluR1 regulating PKC and NMDAR1 in synaptic plasticity variation induced by aluminum treatment**
Ya-qin Li (Shanxi Medical University, Taiyuan, China)

11.05  Discussion

11.10  Platform 17
**Interrelationship between aluminium, silicon and elements associated with tissue metabolism in the degenerated intervertebral disc in patients treated surgically**
Anetta Zioła-Frankowska (Adam Mickiewicz University in Poznan, Poland)

11.30 Discussion

11.40  Platform 18
**Role of aluminium in human chronic poisoning by toxic metals**
Maria Elena Ferrero (University of the Study of Milan, Italy)

12.00  Discussion

12.10  Platform 19*
**Urinary excretion of aluminium and silicon in newborn infants**
Isabel Rodriguez (Keele University, United Kingdom)

12.30 Discussion

12.40 Oral Poster 9*
**Impact of aluminum on sperm DNA quality**
Mohamed Ghazi (CHU de Saint-Etienne, France)

12.45  Discussion

12.50  Oral Poster 10
**New type of cigarettes IQOS as a possible source of body burden by risk elements**
Ondřej Drábek (Czech University of Life Sciences Prague, Czech)

12.55  Discussion

13.00  Short Video
**Our daily aluminium**
Karin Iková (Secondary Vocational School, Hlohovec, Slovakia)
13.10  **LUNCH**

**FREE AFTERNOON**

**Excursion to Uxmal**

20.00  **DINNER**

*Tuesday 26th March 2019*

**Session 4**

**Aluminium and Neurological Disease**

*Denotes presentation by a student.

Chair: Xabier Lopez (*University of San Sebastian, Donostia, Spain*)

8.25  Introduction by the Chair

8.30  Platform 20*

*After the dust settles: A qualitative descriptive study of underground workers who received aluminum dust prophylaxis*

Danielle Aubin (*Laurentian University, Canada*)

08.50  Discussion

09.00  Platform 21

**Aluminum in neurological and neurodegenerative disease; a tribute to the work of the late DRC McLachlan**

Walter Lukiw (*LSU Health Sciences Center, New Orleans, USA*)

09.20  Discussion

09.30  Platform 22

**Aluminium in the pathogenesis of Parkinson’s disease**

Sakae Yumoto (*Yumoto Institute of Neurology, Japan*)

09.50  Discussion
10.00  Platform 23
**Visualising aluminium in the human brain across complex neurological disorders**
Matthew Mold (*Keele University, United Kingdom*)

10.20  Discussion

10.30  **COFFEE**

**Session 5**

**Aluminium Adjuvants, Vaccines and Adverse Events**

*Denotes presentation by a student.
#Denotes 15min. (10+5) Platform Presentation.
$Denotes 20min. (15+5) Platform Presentation.

Chair: Claire Dwoskin (*CMSRI, Washington DC, USA*)

10.55  Introduction by the chair

11.00  Platform 24
*Aluminium is toxic!*
Christopher Exley (*Keele University, United Kingdom*)

11.20  Discussion

11.30  Platform 25
Early life injection of whole vaccines vs the aluminum adjuvant leads to differential behavioral outcomes in mice
Housam Eidi (*University of British Columbia, Vancouver, Canada*)

11.50  Discussion

12.00  Platform 26*#
*Presence of small ruminant lentiviruses in aluminium-induced, post-vaccination granulomas in sheep*
Ricardo de Miguel (*Department of Animal Pathology, University of Zaragoza, Spain*)

12.10  Discussion

12.15  Platform 27*#
*Presence of aluminium in central nervous system of sheep repetitively inoculated with aluminium-adjuvants*
Javier Asín (*Department of Animal Pathology, University of Zaragoza, Spain*)
12.25 Discussion

12.30 Platform 28
Aluminium adjuvant disease in sheep (ovine ASIA syndrome): Implications for human vaccination
Lluis Luján (Department of Animal Pathology, University of Zaragoza, Spain)

12.50 Discussion

13.00 LUNCH

14.20 Platform 29
Assessment of the long-term survival rate of differentiated macrophages exposed to aluminium adjuvants in vitro.
Emma Shardlow (Keele University, United Kingdom)

14.40 Discussion

14.50 Platform 30
Contribution of 18F-FDG PET brain functional imaging for diagnosing aluminium hydroxide-induced macrophagic myofasciitis
Jérôme Authier (Paris Est Creteil University, Creteil, France)

15.10 Discussion

15.20 Platform 31$
Aluminum adjuvants may cause neurological disorders by inducing chronic cytokine expression in the brain
Dan Steinberg (Blogger at VaccinePapers.org)

15.35 Discussion

15.40 Platform 32$
The association between HPV vaccine and lowered fertility
Gayle DeLong (City University of New York, NewYork, USA)

15.55 Discussion

16.00 Platform 33$
HPV: A personal perspective
Sesilje Bondo Petersen (Bispebjerg Hospital, Copenhagen, Denmark)

16.15 Discussion

16.20 Platform 34$
From The HPV Vaccine on Trial: concerns regarding aluminium-based adjuvants in human papillomavirus vaccines
Kim Mack Rosenberg, Esq (Bouer Law, LLC, New York, New York, USA)

16.35 Discussion
16.40 Platform 35
Global vaccine safety and policy shortcomings
Del Bigtree (Informed Consent Action Network)

17.00 Discussion

17.10 Platform 36# (Film)
Under the skin – The sheep experiment: Outtake of an upcoming documentary film
Bert Ehgartner (Vienna, Austria)

17.20 Discussion

17.25 TEA

Final Session Chair
Christopher Exley (Keele University, United Kingdom)

JD Birchall Lecture

Charles T. Driscoll (Syracuse University, New York, USA)

17.45 Introduction by Chair

Effects of acid deposition on the biogeochemistry and toxicity of aluminum and its recovery

18.45 Discussion

18.55 CONCLUSION OF MEETING

20.00 Conference Dinner
Announcements and Prizes!
List of Additional Posters

*Denotes presentation by a student.

Poster 1
The influence of land-use on tropical soil chemical characteristics with emphasis to aluminium
Ondřej Drábek (Czech University of Life Sciences, Prague, Czech)

Poster 2*
Effect of salicylic acid in response to aluminum toxicity in cellular suspensions of Capsicum chinense Jacq.
Yahaira Cab-Guillén (CICY, Mexico)

Poster 3
Relationship between phospholipases C in Coffea arabica phosphoinositide pathways under aluminum stress
Armando Muñoz Sanchez (CICY, Mexico)

Poster 4*
Aluminum at acidic pH induces the resistance of Capsicum chinense to Pythium ultimum
Normig Zoghbi-Rodríguez (CICY, Mexico)

Poster 5
Aluminum induces deficits in the expression of multiple essential cytoskeletal and synaptic elements in human neuronal-glial (HNG) cells primary co-culture
Walter Lukiw (LSU Neuroscience Center, New Orleans, USA)

Poster 6
Effects of aluminum chloride on proliferation and neurogliogenesis of neural progenitor cells
Vera Morsch (Federal University Santa Maria, Brazil)

Poster 7*
Our daily aluminium
Karin Iková (Secondary Vocational School, Hlohovec, Slovakia)

Poster 8*
Observation of potential genotoxic properties of aluminium ions
Dominik Juračka (Comenius University in Bratislava, Slovakia)
Silicic acid

Christopher Exley

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In the beginning there was……yes, that is right, silicic acid! In this talk I will make the case for silicic acid being the second most important molecule on Earth after water. I will define silicic acid and briefly delineate its extremely limited chemistry, at least in the context of life on Earth. I will show how its presence has always been critical in keeping aluminium out of biota. How its role in biological silicification has influenced the success of many plants and how biological silicification has been at the heart of silicic acid as Earth’s thermostat. The latter demonstrating the role of the silicic acid cycle in climate change. The aluminium age is challenging the beneficence of silicic acid in ways that the remainder of Keele13 will outline and discuss.
Interaction of aluminum and silica with anaerobic acidophiles: A geochemical perspective with emphasis on biomineralization

Javier Sánchez-España1, Iñaki Yusta2, William D. Burgos3

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In acidic environments (e.g., volcanic crater lakes, pit lakes, acid mine drainage), dissolved aluminium and silica may be present at very high levels. The concentration of Al$^{3+}$ can be high enough to be poisonous for many microorganisms, so its mobility and interaction with microbes becomes of major importance. The microscopic examination of planktonic microorganisms present in deep anoxic layers of acid pit lakes in SW Spain has shown aluminium and silica incorporation in acidophilic microorganisms1. Analyses by electron microscopy (FESEM-EDS, S/TEM-EELS, TEM) reveals cocci and rod-like cells mineralized by amorphous aluminosilicate and coated by an outermost nanometric layer of adsorbed ferrous iron (Fe[II]). Whether this mineral precipitation is merely a passive process in dead cells (i.e., permineralization) or represents an adaptive mechanism of detoxification in viable cells (e.g., by surface-catalyzed precipitation and/or biosorption) is currently unknown. On-going omics-based studies2 will help deciphering the possible microbial roles on the biomineralization process.


This work has been funded by the Spanish Ministry of Science, Innovation and Universities (grant number CGL2016-74984-R).
New evidence for the Iron-Aluminum Hypothesis (Al could play an important role in the ocean carbon cycle and climate change)

Linbin Zhou

CAS Key Laboratory of Tropical Marine Bio-resources and Ecology, South China Sea Institute of Oceanology, Chinese Academy of Sciences, Guangzhou, China

Effects of aluminum (Al) on marine organisms have been attracting increasing attention in recent years. Recent studies show that Al could be beneficial to the growth of marine phytoplankton through facilitating the utilization of dissolved organic phosphorus, iron (Fe), and dinitrogen (N$_2$). It can also influence the decay of biogenic matter. On the basis of these knowledges, we have proposed the Iron-Aluminum Hypothesis, which delivers the idea that Al, through enhancing the carbon fixation in the upper ocean, and facilitating the export and sequestration of the fixed carbon to ocean depths, could play an important role in the ocean carbon cycle and climate change. In this presentation, I will talk about our new results on the uptake and subcellular distribution of Al in marine phytoplankton, and the effects of Al on the carbon fixation of four marine phytoplankton species (3 diatoms and one cyanobacteria) and the decay of the fixed organic carbon by using the radiocarbon ($^{14}$C). Our results provide strong evidence that marine diatom can uptake and internalize Al into their cells, with a rate comparable to the internalization flux of Fe to the same diatom.

Once being assimilated, Al was partitioned to subcellular components in the following order: granules (69 ± 5%) > debris (17 ± 4%) > organelles (12 ± 2%) > heat-stable peptides (HSP) (~2%) > heat-denaturable proteins (HDP) (< 1%), indicating that the majority of intracellular Al was detoxified and stored in inorganic forms, and substantial Al was further transported to organelles (e.g. chloroplast). Being consistent with our previous results, the presence of Al enhanced the carbon fixation by the tested marine phytoplankton species. More importantly, our results for the first time showed that the presence of Al in environmentally relevant low levels (40 nM to 200 nM) could significantly reduce the decay of the phytoplankton-fixed organic carbon in seawater media both with and without bacteria. These results provide new evidence for the Iron-Aluminum Hypothesis.
PLATFORM 4

The influence of soil vegetation cover and precipitation on soil aluminium pools

Petra Vokurková¹, Václav Tejnecký¹, Naďa Řeřichová¹, Monika Hradilová¹, Karel Němeček¹, Luboš Borůvka¹ and Ondřej Drábek¹

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Composition of tree species is a primary characteristic of forest ecosystems, it influences directly the cycling of chemical elements due their litter. Two study plots with identical geological, climatic and geographical conditions in a heavily acidified region of the Jizera Mountains, Czech Republic, were selected. The only difference were contrasting vegetation covers consisting of European beech (Fagus sylvatica L.) and Norway spruce (Picea abies (L) Karst.). We monitored inputs to soils (litter fall and precipitation) and also the dynamics of litter decomposition was studied by means of a “litter bag” experiment.

The soil profiles, under each vegetation type, were sampled in all diagnostic horizons (L, F, H, A and B) and analyzed in details. The different Al pools (non-crystalline and water soluble) were calculated using determined soil bulk density. Faster decomposition of beech litter compared to spruce litter was observed, however, the content of Al increased in litter residues for both types. The Al pools are comparable in upper layers under both soil vegetation covers, however, the bottom part of soil profile under spruce exhibited a significant Al enrichment - probably due to podsolization processes. This fact points on a possible future damage of spruce forest due to Al stress.
Changes in low molecular weight organic acid production as indicators of fungal response to aluminium stress

Filip Polák¹,², Martin Urík¹,², Marek Bujdoš¹,², Peter Matúš¹,²

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This contribution investigates Aspergillus niger’s behaviour in presence of the mobile aluminium(III) by evaluating the minute changes in H⁺ and oxalate exudation. By comparison of the fungal activity (1) at various initial aluminium concentrations, and (2) at presence of various natural aluminium chelators (e.g. humic acids) affecting aluminium mobility, we have evaluated fungal response to increased aluminium bioavailability. Our results indicate that efficiency of H⁺ and oxalate exudation as well as gluconate uptake by the fungus change significantly in few hours after the aluminium exposure. These findings led us to conclusion that the changes in oxalate and H⁺ production as well as in the gluconate consumption represents Aspergillus niger’s form of stress response to aluminium bioavailability increase.

The financial support was provided by VEGA 1/0146/18 and 1/0354/19, and Slovak Spectroscopic Society, member of the Association of Slovak Scientific and Technological Societies with following logo:
ORAL POSTER 1

Effect of aluminum on the growth, sporulation and virulence of Pythium ultimum


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Soil contamination by aluminum (Al) represents a limitation for agricultural production. When pH in soils decreases lower than 5, Al is solubilized to its trivalent toxic form (Al$^{3+}$), which affects the growth and development of the plants. Additionally, Al could also modify the metabolism of pathogenic organisms and that would explain why, despite being a cosmopolitan pathogen, it does not affect all soils for agricultural uses in the same way. Pythium ultimum is an oomycete that is a phytopathogenic that causes annual agroeconomic losses and affects the genus Capsicum. To study the effect of aluminum in this pathogenic species, it is proposed to evaluate the growth, sporulation and virulence of P. ultimum with 100 μM of AlCl$_3$ in potato dextrose agar medium at pH 4.3, to elucidate some changes in this oomycete due to the toxicity of the aluminum at acid pH.

The research is financed by the project No. 35 of Science Frontiers (SMTHS) and the scholarship of CONACYT # 622192 for NMZR.
Aluminum exposure in honey bees: effects on forage, lifespan, and the cholinergic system

Ana M. Chicas-Mosier¹, Charles I. Abramson²

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²Oklahoma State University Department of Psychology

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Poor mining practices and soil acidification increase bioavailability and uptake of aluminum by flora¹. Plant products such as pollen and nectar are then ingested by honey bees and stored in the hive where bioaccumulation can occur². This presentation focuses on the free-flight and captive responses of honey bees to aluminum exposure. Using free-flight experiments such as artificial flower patches and floral nectary analogs we have determined how choice and flight times vary after exposure³. Additionally, captive experiments have shown that circadian rhythmicity is unstable, bees are hyperactive, and that exposure decreases lifespan. These data has been corroborated by bee-head acetylcholinesterase concentrations and suggest a hormetic tendency of the metal. The severity of these responses are tied to subspecies but effects have occurred across Apis mellifera. We conclude that aluminum exposure from floral products is likely a limiting factor to pollinator health and may contribute to pollinator decline.


Acknowledgements and Funding: This research was funded in part by National Science Foundation Programs including the Graduate Research Fellowship Program (#1144467), Research Experiences for Undergraduates (DBI 1560389), Partnership for International Research and Education (OISE 1545803), Louis Stokes Alliance for Minority Participation Bridge to the Doctorate (#HRD-1612560) and Centers of Research Excellence in Science and Technology: Puerto Rico Center for Environmental Neuroscience (#HRD-1736019). We would like to thank several individuals for their participation in data collection for this project including Timothy Black, Charles Cirocco, Kelly Barretto, Samuel Alvarado, Melina Pérez, Alexander Melendez and Janpierre Alemán-Ríos.
The effect of river water acidity and aluminium on boreal fish assemblages and fish kills

Tapio Sutela and Teppo Vehanen

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In Europe, the largest acid sulphate soil areas are found in western Finland. Riverine fish assemblages in this area were sampled with electrofishing. The lowest average pH (4.55) values and the highest average total Al concentrations (7.4 mg l\(^{-1}\)) were recorded in the river Vöyrinjoki, which appeared to be fishless. Frequency of sites with no fish was highest (59 %) in rivers with average pH < 5. Acid-sensitive species, especially grayling (Thymallus thymallus), brown trout (Salmo trutta) and Eurasian minnow (Phoxinus phoxinus), were usually not found in rivers with average pH < 6 and total Al > 0.8 mg/l. Tolerant fish species, pike (Esox lucius) and perch (Perca fluviatilis), were recorded even in rivers with an average pH of 4.6 and total Al 3 mg/l. Fish-based bioassessment indicated worst ecological status in the most acidified rivers. Documented fish kills supported the concept of acidity and Al as essential drivers of fish assemblages.

Acknowledgements: This study was part of the EU Life+ funded project CATERMASS and the EU-project HaKu.
Foliar aluminum concentration of Central America tree species

Alfredo Alvarado-Hernández\textsuperscript{a}, Ronald Chaves-Corea\textsuperscript{a}, and Eduardo Chacón-Madrigal\textsuperscript{b}

\textsuperscript{a} Universidad de Costa Rica, Centro de Investigaciones Agronómicas, Facultad de Agronomía, San José, Costa Rica. C.P. 2060.
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Foliar concentration for 200 species collected from natural forests and plantations are presented and a total of 3559 samples were analyzed for N-P-K-Ca-Mg-S-Fe-Mn-Zn-B-Cu-Al and Na. Foliar Al concentration varied between 3 and 31 328 mg Al kg\textsuperscript{-1}, and species were grouped (mg kg\textsuperscript{-1}) as non-accumulators (<100, \textit{n}=104), generalists (100-1000, \textit{n}=75), accumulators (1001-10 000, \textit{n}=13) and hyper-accumulators (>10 000, \textit{n}=8). Only 21 species of the families Melastomaceae, Vochysiaceae, Rubiaceae, Cornaceae presented Al value over a 1000 mg kg\textsuperscript{-1}.

Only 7 accumulators and hyper-accumulators species of the genera Vochysiaceae, Melastomaceae, and Rubiaceae presented the micronutrient foliar concentration tendency Al>Na>Mn>Fe>B>Zn>Cu (\textit{Vochysia guatemalensis}, \textit{Faramea permagifolia}, \textit{Mouriri sp.}, and \textit{Faramea occidentalis}, and \textit{Blakea sp.}), and 3 species that belonging to the Fabaceae and Ulticaceae families (no-accumulators and hypo-accumulators, with the exception of the accumulator \textit{Conostelgia xalapensis}) followed the sequence Al>Fe>Mn>Na>B>Zn>Cu (\textit{Conostelgia xalapensis}, \textit{Penthaclethra macroloba}, \textit{Lonchocarpus minimiformis}, and \textit{Cecropia peltata}).

Project partially financed by the International Plant Nutrition Institute (Dr. Raúl Jaramillo) and the Centro de Investigaciones Agronómicas.
Aluminium and phosphorus availability to tea plants (*Camellia sinensis*) influences leaf polyphenol patterns

Roser Tolrà¹, Roghieh Hajiboland², Charlotte Poschenrieder¹

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Tea (*Camellia sinensis*) is an Al hyperaccumulating species. Bioavailability of this tealeaf Al seems relatively low. Although, long-term body accumulation in massive tea consumers cannot be ruled out. High leaf concentrations of polyphenolic substances may contribute to Al binding in tea infusions thus reducing health risks. Moreover, the catechin-type phenolics in tea have antioxidant properties that are beneficial for human health. The purpose of this study was to evaluate the influence of differences in aluminium and phosphorous availability on polyphenol patterns in young and old tealeaves, along with the Al-induced changes in leaf mineral nutrients. Both Al supply and leaf age influenced catechin-type phenolics and significant interactions between Al and P supply on leaf epicatechingallate (ECG) levels, were observed. Leaf Fe concentrations were negatively correlated to leaf ECG. Tea plantation management may largely influence polyphenolic concentrations in tealeaves and, in consequence, modulate the beneficial and detrimental effects of tea consumption.

Acknowledgement: Supported by Spanish MICINN BFU2010-14873/subprogram BFI.
Interactions of aluminum in algae and plants: Elucidating aluminum accumulation in plants by mapping techniques

Ku-González Angela¹, Sánchez-Rodríguez Esteban², Martínez-Estévez Manuel¹, Bojórquez-Quintal Emanuel²

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In plants and other organisms, aluminum (Al) can have a beneficial or toxic effect depending on factors such as metal concentration, the chemical form of Al, growth conditions, plant species and accumulation in tissue plants. Indeed, understanding the distribution of Al within plant tissues is important across a range of fields in plant tolerance science. In this work, the mapping techniques —confocal microscopy and SEM-EDS-FRX— were used to determine the location of Al in tissue the different plants species, providing in situ information the Al-accumulation. Confocal microscopy images indicated the location of the aluminum in the nucleus and small intracellular compartment such as vesicles. In SEM-EDS-FRX images was observed the distribution the Al in different tissue and organs plants. Thus, mapping techniques can play a key role in answering questions on Al-homeostasis in plants from the roots and shoots tissues.
Studies on Al-tolerance mechanisms in seedlings of *Fagopyrum esculentum* Moench

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Our studies are focused on the understanding of the mechanisms that provide Aluminum (Al) tolerance to *Fagopyrum esculentum*. This Polygonaceae is an Al-tolerant plant, however the mechanisms of how this plant, at the early stages, copes with this metal are not fully understood. Previous studies have shown that radicle growth is inhibited at early times, but recovering its growth rate later. We have performed molecular transcriptomic analyses to explore for candidate genes, and to evaluate if the antioxidant system and ABA are involved in these early mechanisms. Genes related with transport, cell wall, and hormone are expressed during 24 and 48-h of Al-treatment. Besides, ABA levels increased and it might be involved in regulating the activity of antioxidant enzymes during the first 48-h Al-treatment. Our results add new information on the transcriptomic profile as well as the role of ABA and antioxidant systems of Al-exposure at early times of *F. esculentum*. 
Wild rice *Oryza glumaepatula* as a new source of aluminum tolerance genes for improving yields of cultivated *Oryza sativa* in acid soils

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Aluminium (Al) toxicity is the primary factor limiting crop growth and yield in acid soils¹. Rice (*Oryza sativa* L) exhibit the highest Al-tolerance among cereals². However, there is interest in improving its tolerance through gene discovering and molecular breeding. *Oryza glumaepatula* Steud. is a wild rice species distributed in Central and South America³, able to grow under acidic and alumino-toxic soils⁴. Through an Al-response screening of an *O.glumaepatula* collection, we identified genotypes, such as OG89, with higher growth rates than cv. Azucena, an *O.sativa* cultivar tolerant to Al. Chemical and molecular analyses suggest that internal detoxification and exclusion mechanisms play essential roles in OG89 tolerance. Metal transporters, organic acids and cell-wall-remodeling-proteins are the main factors involved in its Al-response. By comparing with Azucena, there are either common⁵ and novel mechanisms conferring Al-tolerance to OG89, which position *O.glumaepatula* as a new promising source of genes for improving Al-tolerance in cultivated rice.


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Study of aluminium toxicity effect on secondary metabolites production and signal transduction mechanisms in two suspension cells cultures

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Aluminium (Al) is the most abundant metal on Earth. It represents 7% of all elements. The toxicity produced by this metal is widely documented in tropical acid mineral soils. It is the major factor limiting the productivity of crop species. Coffee is one of the most economically important crops worldwide, mainly due to the production of the secondary metabolite caffeine. In the other hand, the fruits of the habanero chili pepper belong to the species Capsicum chinense Jacq. Habanero chilies are relevant for the economy due to their high demand and agricultural production. However, this crop, as well as coffee are affected by different types of biotic and abiotic stress. In the present work the effect of Al on these two crops, coffee and chili pepper, was studied. We have developed a biological model in which suspension cells of Coffea arabica and Capsicum chinense have been used. We found that aluminium toxicity affected caffeine and phenylpropanoids’ production. In addition, the signal transduction mechanisms through which the signalling molecules associated to the phosphoinositide signalling pathway are affected by the Al stress, was studied. An overview of the latest results will be presented.

Research founded by CONACYT (219893, IFC 2015/035).
ORAL POSTER 4

Aluminum modifies the protein binding of different molecular species of phosphatidic acid in suspension cells of Coffea arabica L.

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Aluminum stress could provoke severe adverse effects in plants of agronomic importance. When the soil solution reaches pH values lower than 5, this metal is solubilized as Al³⁺ producing toxic effects in plants, such as a limitation in root growing. The understanding of the Al³⁺ toxicity mechanisms at cellular level could turn into a valuable tool for biotechnological improvement to this stress condition. Previous reports have demonstrated that Al displays a strong interaction with the negatively charged plasmatic membrane, leading to its depolarization. Also, Al could affect the phospholipidic signaling cascade altering phosphatidic acid (PA) biosynthesis and disturbing, in this way, the lipid mediated stress response¹. We are currently studying the lipid mediated response to Al using in vitro cell cultures of Coffea arabica, a susceptible crop to this metal. By exposing cultures to AlCl₃ 500 µM, we identified a time dependent modification of the different molecular species of PA, identifying specific proteins that interact with these lipids as well.


This work is funded by the project No. 219893 (SMTHS) and the scholarship of CONACyT #37938 to RJPK.
Effect of the nitrogen source on aluminium toxicity in suspensions cells of *Coffea arabica* L.

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Agricultural soils with an acidic condition, that favors Al toxicity, are a problem in the cultivation of coffee plants, as they affect their quality and productivity¹. In addition, the availability of nutrients in the environment, such as N, is also affected by the degree of acidity and the conditions in which it is found². In the present work we studied the effect of the N source on the toxicity by Al in the model of suspensions cells of *Coffea arabica* L. The results indicated that when the *C. arabica* L cells were cultured in NO₃⁻ containing medium, they were not affected by Al toxicity. The free Al content and their intracellular level also decreased in the cells under this N condition. On the other hand, the cells of 14 days cultured in the medium modified with NO₃⁻ presented an increase in the content of NO₃⁻, compared to the control cells, and this were not affected when the cell suspensions treated with AlCl₃. We concluded that the N source does affect the toxicity by Al in suspensions cells of *C. arabica* L.


Project funded by CONACYT (219893) to SMTH-S, the scholarship number 89292 and “beca mixta” from CONACYT to JC-S.
Nitrate reductase-dependent nitric oxide production is involved in the response to aluminum stress in *Coffea arabica* L. suspension cells

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Aluminum toxicity modifies a wide range of physiological, cellular and molecular processes, but the mechanisms underlying plant responses to Al³⁺ toxicity remain elusive. Nitric oxide has been considered an important signaling molecule involved in plants’ responses to biotic and abiotic stresses. Potential changes in endogenous NO levels in response to aluminum stress may be involved. The goal of this work was to evaluate whether the enzymatic activity of nitrate reductase (NR)-dependent nitric oxide production may be required in the response to aluminum stress. We have generated two *C. arabica* cell lines, which are maintained: one in the light (L2RM, 8.3 W/m²) and the other, in the dark (L2). We treated both cell lines with 500 μM AlCl₃ for 7 days and observed an important decrease (50%) in growth cell, but an enhancement of NR activity. Using NO donors, NO scavengers and NR inhibitors, we are trying to determine if changes in NO levels are involved in Al-induced physiological responses.

This work is funded by projects No. 219893 from Conacyt to S.M.T. H-S and and 308112 scholarship to L.Y. E-H.
Role of salicylic acid induced phenylpropanoids in response to aluminum stress in *Capsicum chinense* cell cultures.

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Plants are often exposed to an Aluminum (Al) environment in soil. However, when soil pH decreases, Al is transformed into trivalent cation which can be absorbed by plants, causing numerous disturbances in plant organs and tissues. As an important signaling molecule, salicylic acid (SA) regulates plant growth and development by inducing the response on plants’ defenses. This may be involved in response to Al stress.

We demonstrated in *C. chinense* suspension cells that the exogenous addition of SA stimulates the enzymatic activity of phenylalanine ammonia lyase (PAL), a key enzyme in plants from which various secondary metabolites derive. We treated the cell line with AlCl₃ prior to treatment with SA, and observed an increase in PAL activity and enhancement in the accumulation of phenylpropanoids. The results will be presented and discuss the possible role of SA induced phenylpropanoids biosynthesis in the protection of *C. chinense* cells from Al responses.

This work is supported by the grant No. 219893 from CONACyT to SMTHS and the scholarship No. 588939 from CONACyT to IMVP.
Computational Approach to Aluminum Biochemistry: How aluminum can alter the thermodynamics of redox reactions.

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It is well known that aluminum can alter the thermodynamics of key redox reactions in biological systems and promote oxidative stress. In the present work, we show how a computational approach can be used to unveil the mechanism by which aluminum can alter redox reactions in biological systems. We will revise some of our previous work on aluminum promotion of Fenton reactions, showing how the presence of chelating agents such as citrate can alter the corresponding redox equilibria and the stabilization of aluminum-superoxide compounds. Besides, we analyze recent evidences found in the literature, where it is shown that the presence of aluminum can promote radical scavenging reactions, finding a good agreement between theory and experiment. Our calculations reveal how the stabilization of anionic Reactive Oxygen/Nitrogen Species is a key aspect in the influence of aluminum in the equilibria in which ROS's participate, leading to alteration of the concentration of radicals in biological systems.
Speciation analysis of aluminium organic complexes, method development and application in food analysis

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Aluminium speciation is a difficult task for analytical chemistry. The research presents the method development for speciation both inorganic and organic aluminium complexes in model solution by HPLC-ICP-MS. For this purpose the different solutions with variable pH values, molar ratio Al/Ligand and separation temperature were used. Separation was performed based on isocratic and gradient elution with the use of cation exchange (material: PSDVB/Sulfonic Acid). All determinations were confirmed based on offline tools: Ion Chromatography, FISE and ICP-MS methods and confirmed by chemical equilibrium modelling programs. The developed methods for speciation analysis of aluminium allowed to determine the aluminium complexes with charge +1, 0, -1, +2 and 3+ form during one analysis in the form of both inorganic as well as organic complexes. The new method has been successfully applied first time in speciation analysis of wine samples.

The research was financed by the Faculty of Chemistry, Adam Mickiewicz University and National Science Centre in Poland.
Aluminium chloride triggers neuroinflammation \textit{in vitro} on microglial cells: possible involvement of the purinergic system

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Neuroinflammation is considered one of the current hallmarks for the development of Alzheimer’s disease, and aluminium (Al) could be implicated in this process. Once the immune system is closely related to the purinergic system, this one could also be involved in the course of neuroinflammation. Thus, we evaluated the effect of Al concentrations (1-1000 µM) on the proliferation, morphology, apoptosis, NTPDase, and 5’-nucleotidase enzymes activity of microglial cells after 96h. Al at higher concentrations (500 and 1000 µM) increased cell proliferation with significant changes in cell morphology, and also increasing apoptotic events. In relation to purinergic system enzymes activities, Al decreased ATP and ADP hydrolysis (NTPDase), and AMP hydrolysis (5’-nucleotidase). In conclusion, Al triggered an inflammatory process on microglial cells with the possible involvement of the purinergic system. The role of receptors and signaling molecules still needs to be addressed to better elucidate the effects of Al.

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Role of LncRNA BACE1-AS on regulating Aβ in neuronal injury induced by aluminum exposure

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Objective: To explore the role of LncRNA BACE1-AS in aluminum-induced amyloid beta (Aβ) deposition in vitro, and to propose a new mechanism of aluminum-induced neuronal damage.

Methods and materials: As an experimental model, SH-SY5Y cells were exposed to AlCl₃ at concentrations of 0, 125, 250, 500 μmol/L for 24 h. Cell viability, necrosis, apoptosis and changes in intracellular reactive oxygen species (ROS) were detected by Cell Counting Kit-8 (CCK-8), Lactate Dehydrogenase (LDH), FITC-Annexin V/PI and Dichloro-Dihydro-Fluorescein Diacetate (DCFH-DA). The localization of LncRNA BACE1-AS was detected by LncRNA fluorescence in situ hybridization (FISH). The LncRNA BACE1-AS or miR29a low expression model was established by small interfering RNA (siRNA) technique. The expression of beta-secretase1 (BACE1) and miR29a was detected by q-PCR and Western blot. The localization and expression of Aβ in the cells were detected by immunofluorescence and ELISA Kit.

Results: Result showed that with the increased concentration of AlCl₃, cell necrosis and apoptosis were observed, and intracellular ROS and Aβ level were increased. LncRNA BACE1-AS expression and BACE1 expression (RNA and protein) was increased, while miR29a expression was decreased compared with the control group. Indeed, LncRNA BACE1-AS bound to and attenuated miR29a expression, and the BACE1-AS single knockdown inhibited BACE1 RNA and protein expression and Aβ production; however, the double knockdown caused BACE1 to exceed control levels and exacerbated Aβ production, these interactions were enhanced by AlCl₃.

Conclusion: Aluminum up-regulated the expression of LncRNA BACE1-AS, which competitively bound to miR29a, resulting in increased expression of BACE1 and increased Aβ production, leading to neuronal damage.

Keywords: Aluminum; siRNA; LncRNA BACE1-AS; miR29a

Funding references National Natural Science Foundation of China (81430078, 81703202)
Effect of MLL modified H3K4me3 on aluminum induced cognitive impairment—Both population and animal epigenetic studies
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Objective: Epigenetic modifications play critical roles in cognitive function. Brain-derived neurotrophic factor (BDNF) is involved in synaptic plasticity and may be modified by tri-methyl histone H3 lysine residues 4 points (H3K4me3), which may be modified by mixed-lineage leukemia protein (MLL), a zinc finger-rich enzyme, thus affecting cognition. This study aims to explore mechanism of this epigenetic modification. Methods: 1. 235 male Al-exposed workers were recruited. An occupational epidemiological investigation questionnaire and cognitive tests were performed. The contents of H3K4me3 in lymphocyte and BDNF in plasma were determined by enzyme-linked immunosorbent assay. 2. 24 healthy SD male rats were randomly divided into four groups by weight. The rats drank water containing different doses of aluminum chloride (AlCl3) (0, 2, 12, and 72mg/kg Al3+) for 120d. The neurobehavior of animals was tested, and expression of H3K4me2 and MLL was detected with western blot. Results: 1. With the increasing of blood aluminum level, the cognitive function of Al-exposed workers decreased, The expression levels of H3K4me3 decreased, and BDNF decreased. Multiple correlation analysis showed that Blood aluminum concentration was negatively correlated to H3K4me3, BDNF, and cognitive function, respectively. 2. With the Al dose increasing, the neurobehavior of animals decreased, the expression of MLL and H3K4me3 decreased too. Conclusion: Aluminum inhibits MLL by replacing zinc, then the activity of MLL decreases, the methylation of H3K4 increases, the expression of H3K4me3 decreases, then BDNF decreases.

References

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ORAL POSTER 8

Role of mGluR1 regulating PKC and NMDAR1 in synaptic plasticity variation induced by aluminum treatment

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Objective To study the mechanism of aluminum (Al) regulating protein kinase C (PKC) and N-methyl-D-aspartic acid receptor 1 (NMDAR1) through metabolic glutamate receptor 1 (mGluR1), which results in synaptic plasticity variation, and to preliminarily clarify the neurotoxicity mechanism of aluminum-induced learning and memory disorders.

Methods Rats were treated with 10mM maltol aluminum and mGluR1 agonists or antagonists, long-term potential (LTP) in hippocampus CA1 region were detected to reflect the changes of synaptic plasticity, the expression of mGluR1, PKC and NMDAR1 mRNA and protein were examined by RT-qPCR and Western blot.

Results The results showed that mGluR1 inhibited LTP in hippocampus CA1 region. Meanwhile the expression of PKC and NMDAR1 showed an opposite trend to that of mGluR1 after treating with mGluR1 agonists or antagonists.

Conclusion Aluminum may decrease the expression of PKC and NMDAR1 by upregulating mGluR1, which causes LTP changes in hippocampus CA1 region and leads to changes in learning and memory.

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Interrelationship between aluminium, silicon and elements associated with tissue metabolism in the degenerated intervertebral disc in patients treated surgically

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The spine degenerative disease begins within the intervertebral disc (IVD). Degeneration of IVD is considered an unresolved problem of modern medicine. The main reasons for the IVD degeneration are age, diseases and undergoing operations. However, it is not taken into account what effect the elements, including aluminium, in the disc have or can have. We assumed that, the content of Al and metabolic trace elements may reflect biological processes within the IVD. The analyzed elements were different in terms of chemical and biological characteristics in order to evaluate mutual changes and relationships. The content of the elements were determined by spectrometric methods. We confirmed, for the first time, the similarity between Si and Al for human IVD. We found that, the properties of the end plate most likely allow that aluminium can be transported to the disc regardless of the stage of development and its content may depend on the intensification of metabolic processes within the disc.

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Role of aluminium in human chronic poisoning by toxic metals

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We studied the relationship between toxic metal burden and human diseases on 1147 patients: 338 healthy control and 809 affected by neurodegenerative or other diseases. The patients were subjected to “chelation test” with the chelating agent calcium disodium ethylene-diaminetetraacetic acid (EDTA) in order to verify their possible burden by toxic metals. Twenty-one toxic metals were analyzed: aluminium (Al), antimony, arsenic, barium, beryllium, bismuth, cadmium, cesium, gadolinium, lead, mercury, nickel, palladium, platinum, tellurium, thallium, thorium, tin, titanium, tungsten, and uranium. The analysis was performed in the urine samples of the patients by inductively coupled plasma mass spectrometry. Our results showed that: 1) all patients were affected by toxic metal burden; 2) lead was the most represented toxic metal, followed by cadmium, gadolinium and Al; 3) patients affected by diseases displayed more elevated toxic metal burden than healthy controls. About 24% of total examined patients were affected by Al burden.
**PLATFORM 19**

The contribution of breast and formula feeding to the body burden of aluminium in infants (0-12 months).

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Breastmilk and infant formulas are the only source of nutrition in newborn infants and, the latter in particular, is contaminated by aluminium [1,2]. Exposure to aluminium in infants is associated with anaemia, bone disease and impaired neurological development [3,4]. There are no data on the gastrointestinal absorption of aluminium in newborn infants. A clinical trial was conducted and 23 healthy, term infants were recruited (REC Ref. 14/WM/1114) through Russells Hall Hospital, and spot urine samples were collected from infants at T=0, 3, 6, 9 and 12 months of age. Breast-feeding mothers collected samples of their breast milk. Total aluminium and silicon were measured in urine and breast milk samples by TH GFAAS and urine creatinine was measured by UV/Vis spectrometry. Parents kept a diary of infant feeding including which infant formulas were fed, the aluminium content of the latter were measured [1,2]. This is the first clinical trial to establish the contribution of breast and formula feeding to the body burden of aluminium in infants.


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ORAL POSTER 9

Impact of aluminum on sperm DNA quality

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Between 1950 and 2013, aluminum production was multiplied by thirty in the world \textsuperscript{1}. Today, men's exposure to aluminum, including food products, cosmetics, air and water contamination, and a number of drugs (vaccine, gastric bandages, etc.) has never been so high and should continue to increase. At the same time, we are witnessing a decline in male fertility in Western countries. In this context, several teams, including ours, have studied the impact of aluminum on the fertility of men. These studies have shown that aluminum accumulates in semen and especially in sperm near its DNA \textsuperscript{2}.

Aluminum has already shown that it is capable of damaging the DNA of various cells, especially to increase DNA fragmentation \textsuperscript{3}. We therefore hypothesize that aluminum could lead to increased sperm DNA fragmentation. This would result in a decrease of men fertility and in higher risk of miscarriage. In order to confirm this hypothesis, we measured aluminum in the spermatozoa of 80 patients who perform artificial insemination and correlate this result to their sperm DNA fragmentation. Patients are recruited from the reproductive biology unit of Saint-Etienne University Hospital. Aluminum assays are carried out using an Atomic Absorption Spectrophotometry technique by Prof. Exley at Keele University. Measurements of sperm DNA damage are carried out using flow cytometry by our research team (SAINBIOSE INSERM U1059) at the Medecine Faculty of Saint-Etienne.


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New type of cigarettes IQOS as a possible source of body burden by risk elements

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A new type of cigarettes – the so called IQOS has been introduced into a market. The IQOS cigarettes represent a reportedly healthier alternative for classical cigarettes. This new smoking approach heats the tobacco filing instead of burning it. This contribution assumes that the danger caused by risk elements remain the same, moreover the Al body burden might be increased due to Al foil wrapping of the tobacco in the case of IQOS cigarettes. A simple smoking device that captures smoke and dust particles in an acidified aqueous filter has been constructed and used to simulate smoking process. The classical cigarettes and the new one has been smoked in a single cigarette mode and in a cumulative mode. The content of captured risk elements including Aluminium was analyzed in the aqueous filter and data were compared and evaluated.
After the dust settles: A qualitative descriptive study of underground workers who received aluminum dust prophylaxis

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Background and Objectives
From 1943 to 1980, some underground gold and uranium workers in Ontario, Canada were required to inhale aluminum dust for silicosis prevention. Workers were exposed to the dust for up to 30 minutes daily. This study explored the perceived impact among exposed Northeastern Ontario workers.

Methods
This qualitative descriptive study included 16 respondents who participated in semi-structured individual interviews. All respondents were Northeastern Ontario workers who were exposed to aluminum dust prophylaxis for at least one year. Interviews were transcribed verbatim and analyzed thematically.

Results
Themes that emerged were: 1) compulsory exposure, 2) hesitancy to complain, 3) workers’ trust in companies, 4) physician lack of knowledge about health impact, and 5) concern about their deceased coworkers.

Implications
Workers’ perceived that their long term health was impacted by exposure. The results will be used to inform health and safety policies, industry practices and policies, and to target future related research.

Aluminum in neurological and neurodegenerative disease

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*communicating author; Email: wlukiw@lsuhsc.edu; the research work in this abstract is dedicated to the memory of DRC McLachlan BS, MD, FRSC, Order of Canada, and his lifelong investigation of aluminum in neurobiological systems and aluminum’s potential contribution to the etiology and neuropathology of Alzheimer’s disease.

With continuing cooperation from 18 domestic-and-international brain banks over the last 37-years we have analyzed the aluminum-content of the temporal-lobe neocortex of 511 human female-brain-samples from 16 diverse neurological and neurodegenerative-disorders and age-matched controls. Temporal lobes (Brodmann A20-A22) were selected because of their availability and central-role in cognition and memory-formation. We used the analytical techniques of (i) Zeeman-type-electrothermal-atomic-absorption-spectrophotometry (ETAAS) and (ii) preliminary analysis using the advanced-photon-source (APS) device at the Argonne-National-Laboratory, US Department-of-Energy, University of Chicago IL, USA. Neurological diseases examined were Alzheimer’s disease (AD;N=186), ataxia-Friedreich's type (AFT;N=6), amyotrophic-lateral-sclerosis (ALS;N=16), autism-spectrum-disorder (ASD;N=26), dialysis-dementia-syndrome (DDS;N=27), Down’s-syndrome (DS; trisomy-21;N=24), Huntington’s-chorea (HC;N=15), multiple-infarct-dementia (MID;N=19), multiple sclerosis (MS;N=23), Parkinson’s disease (PD;N=27), prion-disease (PrD;N=11), progressive-multifocal-leuko-encephalopathy (PML;N=11), progressive-supranuclear-palsy (PSP;N=24), schizophrenia (SCZ;N=21), a young-control-group (YCG;N=22) and an-aged-control-group (ACG;N=53). All pathological tissues were diagnosed after extensive-clinical and/or post-mortem examination. Amongst neurological-conditions we found a statistically-significant trend for aluminum to be significantly increased in AD, DS and DDS compared to controls. These results are the largest study of aluminum-association with neurological-neurodegenerative-disease ever undertaken. The results suggest that aluminum’s-association with AD, DD and DS brain tissues may-contribute-to-the-neuropathology of those neurological disorders but may not be a significant-factor in other incapacitating-lethal diseases of the human CNS.

This research work was supported by the National Institutes of Health (NIH), National Eye Institute (NEI) and National Institute of Aging (NIA), Bethesda MD, USA.
Aluminium in the pathogenesis of Parkinson’s disease

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In the brain of patients with Parkinson’s disease (PD), nerve cells located in the substantia nigra pars compacta (SN) degenerate selectively. In this study, we examined elements contained in nerve cells in the SN of PD patients and those of age-matched controls using scanning electron microscopy coupled with energy-dispersive X-ray spectroscopy (SEM-EDS).

We demonstrated that high levels of Al and Fe were colocalized in the nucleus of nerve cells in the SN of the age-matched controls. In contrast, Al and Fe levels measured in the nucleus of nerve cells in the SN of the PD patients were significantly lower than those of age-matched controls.

Oxidation of nuclear DNA has been reported in neurodegenerative diseases, such as Alzheimer’s disease and PD. The pathogenetic mechanism of PD will be discussed.
Human exposure to aluminium has frequently been implicated in neurodegenerative conditions\(^1\). Furthermore, transversely heated graphite furnace atomic absorption spectroscopy (TH-GFAAS) consistently demonstrates high levels of the metal exceeding those amounts thought to be pathologically benign across complex neurological disorders\(^2\). Only until recently have methods developed sufficiently to unequivocally visualise aluminium in human brain tissue. Using the fluorophore lumogallion \([4\text{-chloro-3-(2,4-dihydroxyphenylazo)-2-hydroxybenzene-1-sulphonic acid}]\) and fluorescence microscopy, aluminium produces a characteristic orange fluorescence emission at 590nm, upon excitation at 500nm. These complementary methods have reported upon the intracellular distribution of aluminium in autism spectrum disorder (ASD)\(^3\) versus predominantly extracellular metal deposition as observed in donors with multiple sclerosis (MS)\(^4\) and familial Alzheimer’s disease (fAD)\(^5\). Current investigations of human brain tissue from donors exposed to high levels of aluminium in contaminated drinking water during the Camelford incident in Cornwall in 1988, will act to further our understanding of the effects of aluminium in disease aetiology.


This research was funded by a grant to CE from the Children’s Medical Safety Research Institute (CMSRI). MM is a CMSRI Research Fellow.
Aluminium is toxic!

Christopher Exley

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Where is the science behind the often-heard statement that the aluminium content of a vaccine is as small as to be negligible, for example, as compared to aluminium in the diet? In this talk I will investigate this premise and specifically from the point of view of the content (concentration) of aluminium at the injection site of a vaccine. We will establish the exposure regime at an injection site and compare this with cytotoxicity studies in the published literature for aluminium. Is it really such a ‘small’ amount of aluminium at a vaccine injection site?
Early life injection of whole vaccines vs the aluminum adjuvant leads to differential behavioral outcomes in mice

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In the present study, development, neuromotor behaviours and neurobehavioural abnormalities (NBAs) are evaluated in mice vaccinated and treated with aluminum adjuvant. In treated animals, we observed abnormal repetitive/aggressive-like behaviors, e.g., “barbering”, and NBAs such as decreased sociability and preference for social novelty. Increased anxiety-like behaviours were observed in mice injected with vaccines and aluminum adjuvant compared to controls. Abnormalities in recognition memory were observed only in mice treated with aluminium adjuvant at six months of age. Our data also show a slower acquisition of some neonatal reflexes in vaccine-treated female mice compared to controls. The observed neurodevelopmental alterations did not have a linear relationship with vaccine doses and seem to be transient in age.

These results suggest that follow up studies are required, including detailed histological evaluation of the central nervous system. This analysis is currently ongoing in our laboratory and will be reported in a future communication.

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We thank the Children’s Medical Safety Research Institute (CMSRI) and the Fox Foundation for their financial support.
Presence of small ruminant lentiviruses in aluminium-induced, post-vaccination granulomas in sheep

de Miguel R¹, Echeverría I², Asín J¹, Molín J¹, de Pablo L², Fernández A¹, Lacasta D¹, de Andrés D², Pérez M¹, Luján L¹, Reina R²

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In sheep, aluminium-containing vaccines induce the recruitment of macrophages and formation of granulomas¹. Small ruminant lentiviruses (SRLV) are retroviruses that replicate in activated macrophages². Eleven adult, naturally SRLV-infected sheep were inoculated with eight doses of aluminium-containing vaccines. In vitro cultures of granuloma, spleen, peripheral blood and bronchoalveolar lavage macrophages were established and monitored for retrotranscriptase activity, PCR and virus identification by gag gene sequencing. Immunohistochemistry was also performed with CAEP5A1 monoclonal antibody. SRLV could be detected in post-vaccination granulomas in 5 sheep (45.5%). In three animals, viral sequences in the granuloma were highly divergent compared to sequences isolated elsewhere in the same sheep (compartmentalization). Location of SRLV was mostly associated to Al-containing phagolysosomes. Persistent granulomatous inflammatory reactions induced by vaccines may allow in situ SRLV replication, thus favouring mutation and recombination. The role of Al-induced, post-vaccination granulomas in the spread and pathogenesis of SRLV need to be addressed and considered.


This work was funded by grants from the Spanish Ministry of Economy and Industry (AGL2013-49137-C3-1-R and AGL2013-49137-C3-2-R). De Miguel R is a PhD student funded by the Department of Innovation, Research and University of Aragon.
Presence of aluminium in central nervous system of sheep repetitively inoculated with aluminium-adjuvants

Asín J\(^1\), de Miguel R\(^1\), Rodríguez A\(^1\), Molín J\(^1\), de Andrés D\(^2\), Exley C\(^3\), Pérez M\(^1\), Reina R\(^2\) and Luján L\(^1\)

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Aluminium (Al)-containing adjuvants promote an effective immune response but in sheep, they also induce local granulomatous reactions and accumulate in regional lymph nodes\(^1\). 21 lambs, divided into 3 groups (n=7 each) were inoculated during 15 months with 19 doses of different substances: A) Vaccines containing Al hydroxide; B) Al hydroxide only; C) PBS. Lumbar spinal cord and frontal lobe of the brain were studied by fluorescence microscopy with lumogallion, Graphite Furnace Atomic Absorption Spectroscopy and immunohistochemistry against glial fibrillary acidic protein (GFAP). Groups A and B showed higher Al concentration in spinal cord than group C (p=0.001). Yellowish fluorescence emission (590 nm), typical of Al, was detected as small aggregates associated to myelin sheets. The highest individual measurements were obtained in group B. GFAP was overexpressed in group B compared to group C (p=0.047). In sheep, Al from adjuvants may translocate from subcutaneous tissue to the CNS, inducing astrocyte activation.


This work was funded by grants from the Spanish Ministry of Economy and Industry (AGL2013-49137-C3-1-R and AGL2013-49137-C3-2-R). Asín J is a PhD student funded by the Spanish Ministry of Education, Culture and Sports.
Aluminium adjuvant disease in sheep (ovine ASIA syndrome):
Implications for human vaccination

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Aluminium (Al)-containing adjuvants are widely used in vaccines applied to animals and humans since they promote an unmatched immune response against antigens. The mechanisms for this response are only partially known even though Al adjuvants have been used for almost ninety years. Studies on the role of these adjuvants in sheep have demonstrated constant formation of long-lasting granulomas after inoculation, translocation of Al to the regional lymph and the CNS, induction of danger signals and activation of the immune system, along with inducing profound behavioural changes. These studies attempts to explain a sheep disease using an ovine model, but results may have a wider impact. Formation of granulomas has been described in human and other mammals and -as in sheep- perhaps they are not occasional side effects but constant inflammatory reactions after vaccination, capable of changing the patient’ health status from healthy to sick. Other implications will be further discussed.


This work was funded by grants from the Spanish Ministry of Economy and Industry (AGL2013-49137-C3-1-R, 2-R and 3-R).
Assessment of the long-term survival rate of differentiated macrophages exposed to aluminium adjuvants in vitro.

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Clinical vaccinations often contain inorganic immunopotentiators in the form of aluminium salts, which help to modulate and stimulate the immune response post antigenic challenge. Vaccine priming and the activation of robust adaptive immune responses is heavily reliant on cell-mediated translocation of antigen-adjuvant complexes to the draining lymph nodes. However, the long-term survival rate of antigen presenting cells loaded with adjuvant particles is currently unknown. Differentiated THP-1 macrophages were exposed to low concentrations of commercial aluminium adjuvants and their viability was monitored using a Presto blue and Live/dead cytotoxicity assay. These cells exhibited various degrees of particulate cytoplasmic loading which was dependent on the duration of exposure to adjuvant material and the type aluminium salt used. Prolonged survival rates in vitro could serve to explain the heightened biopersistence and systemic translocation of aluminium adjuvants in vivo.

Funding
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Contribution of $^{18}$F-FDG PET brain functional imaging for diagnosing aluminium hydroxide-induced macrophagic myofasciitis

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Macrophagic myofasciitis (MMF) is characterized by peculiar pattern of cerebral glucose hypometabolism involving occipito-temporal cortex and cerebellum. Aim was to generate and evaluate a support vector machine (SVM) procedure to classify patients between healthy or MMF $^{18}$F-FDG brain profiles. 119 patients with MMF and 64 healthy subjects (HS) were retrospectively analysed (training set: 100 MMF/44 HS; testing set: 19 MMF/20 HS). Training set exhibited the already reported hypometabolism pattern involving occipito-temporal and fronto-parietal cortices, limbic system and cerebellum. The SVM procedure, correctly classified MMF patients of the testing set with following Se, Sp, PPV, NPV and Acc: 89%, 85%, 85%, 89%, and 87%. In conclusion, this original approach could help to classify patients between healthy or MMF metabolic brain profiles using $^{18}$F-FDG-PET. Machine learning algorithms are promising for computer-aided diagnosis but will need further validation in prospective cohorts.
Aluminum adjuvants may cause neurological disorders by inducing chronic cytokine expression in the brain

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Extensive research and an emerging consensus support a central role of neuroinflammation and elevated brain cytokines as a cause of autism and other neurological disorders and mental illnesses. The cytokines IL-6 and IL-17 are implicated in autism; they cause autism-like behaviors and brain injury in animal models, and are linked to autism in humans. Aluminum adjuvants induce inflammation, which is necessary for vaccine efficacy. New and old evidence, taken together, indicates that aluminum adjuvants in infant vaccinations can travel into the brain, and induce a chronic brain inflammation including elevated IL-6 and IL-17. The chronic nature of adjuvant-induced neuroinflammation indicates potential for adverse impacts on many neurodevelopmental processes occurring in the first years of life.

JB Handley and The Dwoskin Foundation paid for the graphic design and printing costs of the two brochures “Vaccines and the Brain” and “Vaccines and Autism”. Vaccine Papers receives no financial support from anyone and does not sell advertising.
The association between HPV vaccine and lowered fertility

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In 2018, I published an article showing a statistical relationship between HPV vaccine uptake and lowered fertility.1 I examined data that represented 8 million U.S. females aged 25 to 29 from 2007 to 2014. Approximately 60% of women who did not receive the HPV vaccine had been pregnant at least once, whereas only 35% who received the shot had ever conceived. If all women surveyed had received the HPV vaccine, the number of women to have ever been pregnant would have fallen by 2 million. Further study is essential to determine the mechanism(s) driving these results. Researchers need to examine the influence of the HPV vaccine’s ingredients – including aluminium, polysorbate 80, and sodium borate – on female fertility.

Funding source: Wasserman Endowment at Baruch College

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As a former study subject in the Danish part of the Gardasil® trial Future II, I got access to detailed trial information on the pre-licensure clinical trials 501-015 and 501-018 from the Danish Medicine Agency and the Danish National Committee on Health Research Ethics. It is evident that the legal certainty for the study subjects was non-compliant as they were recruited on false prerequisites and were misinformed about the safety profile of the vaccine. The study subjects had no opportunity to know the composition of injected test vaccine and placebo. They were wrongly told that the placebo was saline and were not informed about the use of excipients with no safety profile. Furthermore, the Danish Medicine Agency authorized potassium aluminium sulfate and not amorphous aluminium hydroxyphosphate sulfate as the vaccine adjuvant. Based on these new findings, the safety of the Gardasil® vaccine must be reconsidered.
From *The HPV Vaccine on Trial: concerns regarding aluminium-based adjuvants in human papillomavirus vaccines*

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In their investigative work *The HPV Vaccine on Trial: Seeking Justice for a Generation Betrayed* (Skyhorse Pub. Oct. 2018), Holland, Mack Rosenberg, and Iorio explore issues surrounding HPV vaccines, including: clinical trial data, the vaccines’ ingredients, law, marketing, worldwide HPV vaccine programs, cervical cancer, HPV type replacement, and reports of post-vaccination injuries. Here, they will focus on use of novel aluminium-based adjuvants in HPV vaccines: amorphous aluminium hydroxyphosphate sulphate (AAHS) in Merck’s Gardasil, and AS04 (containing aluminium hydroxide) in GlaxoSmithKline’s Cervarix. They will present information concerning use of aluminium-containing controls and adjuvant doses in vaccines themselves in the trials and address the impact of the study design on safety assessments. Topics addressed will include appropriate placebos, reported adverse events, “new medical conditions,” and the vaccine’s adjuvant dose in the youngest Gardasil trial cohort. The authors also will discuss concerns regarding safety of aluminium-based adjuvants generally, and, particularly, AAHS and AS04.
Global vaccine safety and policy shortcomings

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Emmy-Award winning medical journalist, Del Bigtree is a leading advocate and educator in the arena of vaccine safety. His non-profit, the Informed Consent Action Network, has been investigating shortcomings in vaccine safety and policy globally\textsuperscript{12345}. Mr. Bigtree will illustrate shortcomings in vaccine safety and policy presented to the United States Department of Health and Human Services and present shocking testimony from Stanley Plotkin\textsuperscript{6}, the ‘godfather’ of modern vaccines.


This work was funded by several individual donors from the United States.
PLATFORM 36 (FILM)

Under the skin – The sheep experiment: Outtake of an upcoming documentary film (15 min)

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In documentary films - even if they focus on science - it is very uncommon that someone follows a study "live" from the very beginning - without knowing any results. Meeting Lluis Luján and his PhD Student Javier Asin at the 11th Keele Meeting in Lille - I heard of their plans to undertake a very interesting RCT with three groups of sheep following different vaccine schedules (normal vaccines, aluminium adjuvant only and saline placebo). We started filming in January 2016 at the Veterinary University of Zaragoza and we continued till December 2018 - when we did the final interviews after the studies have been published (1,2). Our film delivers the pictures and the background story of an outstanding scientific experience: What do we know about aluminium-adjuvanted vaccines and their various interactions with body tissue and the immune system? What happens under the skin of sheep - and what are the possible implications for humans?


Funding: The film is funded by private grants, subscriptions and loans.
Effects of acid deposition on the biogeochemistry and toxicity of aluminum and its recovery

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Emissions of sulfur dioxide and nitrogen oxides from fossil fuel combustion are oxidized and transported via the atmosphere to remote regions, where they are deposited as strong acids. Acid deposition has impacted terrestrial and aquatic ecosystems in base poor, montane regions of Eastern North America, and Northern and Central Europe and China. Elevated acid deposition in regions has depleted available nutrient cations from soil and mobilized elevated concentrations of dissolved inorganic aluminum from soil to surface waters, with adverse effects on sensitive plants and aquatic organisms. Over past decades, emission controls have been implemented on electric utilities and mobile sources in North America and Europe resulting in marked decreases in acid deposition and initiating ecosystem recovery from acidification. Chemical effects of aquatic resources have responded relatively rapidly, but biological recovery has lagged. Acid deposition has imparted legacy effects on soil which have delayed the recovery of terrestrial aquatic resources.
POSTER 1

The influence of land-use on tropical soil chemical characteristics with emphasis to aluminium

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Composition of soil vegetation cover and land management influence directly the cycling of chemical elements and is a key factor for Al speciation and behavior. At the same time, Al is an important factor limiting the growth of cultural plants. Eight 1 ha plots with identical geological, climatic and geographical conditions were delimited at the North of Congo Basin (near Mbalmayo, Cameroon) in primary and secondary forests, cocoa agroforestry systems and corn field (two plots per habitat). The most important differences between particular habitats comprise vegetation cover and land management. The soil patches (64 per plot) of 1 m² were exchanged between forests and agricultural lands. The soil was moved in two layers, layer A 0-5 cm, and layer B 5-20 cm of depth. Soil from layers A and B was sampled at each soil patch. Every three months, and soil chemical characteristics have been studied. Particular plots differ before all in their pH, content of exchangeable Al and contents of base cations. Specifically, agricultural soils revealed about 2% and 25-40% of exchangeable Al in layer A and B, respectively, while forest soils contained about 30% and 65% of exchangeable Al in layer A and B, respectively.

The soil chemical characteristics clearly develop towards the state of the new site after the translocation. The Al levels reach around 50% of exchangeable Al in layer B in all environments, and exchangeable Al in layer A increased to 10% in agriculture soils and decreased to 20% in forest soils.
POSTER 2

Effect of salicylic acid in response to aluminum toxicity in cellular suspensions of Capsicum chinense Jacq.

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Salicylic acid (SA) is an important molecule that improves the tolerance of plants to aluminum stress (Al³⁺). The objective of this study was to investigate the effects of the exogenous application of SA on: the production of AS, the accumulation of Al³⁺ in cells and the morphological modifications in cell suspensions of Capsicum chinense Jacq. exposed to stress by AlCl₃. It was initially observed that toxicity of Al³⁺ produced 30% reduction in cell growth at the end of its 24-day culture cycle, it also induced damage to cell morphology. But, the exogenous application of SA in the cells of C. chinense under stress by Al³⁺, resulted in a rapid increase in the concentration of endogenous SA and substantially improved the cell morphology. These results indicate that SA can generate tolerance to aluminum toxicity in C. chinense.

This work is funded by the CONACYT project No. 219893 (SMTHS).
POSTER 3

Relationship between phospholipases C in *Coffea arabica* phosphoinositide pathways under aluminum stress

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*Coffea arabica* L. suspension cell culture has been employed to study the phosphoinositide pathway that involves the aluminum stress. Particularly, it was paid attention to Phospholipase type C (PLC), evaluating the PLCs transcription profile in coffee suspension cells from 14 days of culture that were treated with 100 µM AlCl₃ for 30s or 3h. *CaPLC1* and *CaPLC2* did not show changes after the treatment. In contrast, *CaPLC3* and *CaPLC4* showed specific profile, down- and up-regulated, respectively. The coffee PLC´s were obtained by heterologous expression using pColdII vector in *E. coli* BL21star strain. Also, PLCs constructions (promTUB::PLC::mGFP) were obtained to visualize PLCs subcellular localization. When YFP-*PH*₅₅ (PIP₂ biosensor) was transfected into coffee protoplast, a fluorescence signal was shown close to the polar growth point, but in presence of Al³⁺ this signal was not detected. With these data, the PLC role into signal-transduction process in response to aluminum stress should be established.

This work is supported by a CONACYT grant to SMTHS (219893) and a fellowship to VMGM for a postdoctoral training (166897).
**POSTER 4**

*Aluminum at acidic pH induces the resistance of *Capsicum chinense* to *Pythium ultimum*


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Aluminum toxicity and acidity of soils influences the decrease in agricultural productivity. However, it has been described that the aluminum stress condition activates the defense against biotic stress, known as systemic acquired acclimatization (SAA). *Pythium ultimum* oomycete is a phytopathogen species that causes annual agroeconomic losses and affects the genus *Capsicum*. In order to study if aluminum induces cross resistance against *P. ultimum* in *C. chinense*, it is proposed to make a study on *C. chinense* seeds pretreated with 100 μM AlCl$_3$ at pH 4.3 and then challenge them with a mycelium suspension of *P. ultimum*, to evaluate the effect on the characteristics of seeds, seedlings and to analyze the expression of PR1 gene for plant defense, elucidating aspects of the interaction *C. chinense*-*P. ultimum*.

The research is financed by the project No. 35 of Science Frontiers (SMTHS) and the scholarship of CONACYT # 622192 for NMZR.
POSTER 5

Aluminum induces deficits in the expression of multiple essential cytoskeletal and synaptic elements in human neuronal-glial (HNG) cells primary co-culture

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Progressive loss of multiple synaptic signaling elements and neuronal cell atrophy are distinguishing features of Alzheimer’s disease (AD) neuropathology. Using primary cultures of human brain neuronal and glial (HNG) cells and a quartz-microfluidic based DNA oligonucleotide microarray reporter systemS (GeneChip-Generic MicroSystems; Affymetrix-Thermo-Fisher Scientific) in these experiments we have analyzed the effects of nanomolar aluminum (sulfate) and other potentially neurotoxic metals on the expression of a family of interrelated genes that support and maintain neuronal cytoarchitecture, axonal caliber, the intermediate-filament-structured cytoskeleton and multiple pre-synaptic and post-synaptic proteins known to be essential in trans-synaptic signaling and inter-neuronal communication. The ability of aluminum to selectively repress neurofilament-light (NF-L) and SHANK3 gene expression and others was found to be remarkable compared to the actions of other less-bioavailable metals. These unpublished data will be presented detailing the effects of the 7 potential neurotoxic metals tested on the expression of the 12 neuron-enriched cytoskeletal and synaptic elements analyzed.
POSTER 6

Effects of aluminum chloride on proliferation and neurogliogenesis of neural progenitor cells

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Al is considered a neurotoxin and spreads on the most different types of nerve cells, as in neural progenitor cells (NPCs)¹,². Once NPCs play a key role on development and regeneration of brain throughout life, this metal may contribute to neuropathological conditions³,⁴. Here, we evaluated the effects of Al at different concentrations (0.1–100 µM) on proliferation and differentiation of NPCs isolated from embryonic telencephalons, cultured as neurospheres. Our results revealed that Al reduced the proliferation and expansion of neurospheres, inducing apoptosis in these cells. In addition, Al promoted a decrease in the immature neural marker β3-tubulin expression and an increase in glial fibrillary acidic protein expression, impairing the neural fate by blocking neurogenesis and stimulated gliogenesis. Thus, we conclude that Al may have a decisive function in the proliferation of NPCs that directly affects the choice of cells to differentiate in to neurons or glial cells.


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POSTER 7

Our daily aluminium

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Aluminium and its ions have become an inseparable part of our life. We come into contact with aluminium not only as constructional material, but it can be found in foodstuff, cosmetics and in many drugs. However, aluminium is one of the factors affecting the occurrence of neurodegenerative diseases and breast cancer. The aim of the work was to analyse the samples of commonly used products. 102 samples were measured by AAS and in 25 samples the concentration of aluminium was higher than 850 μg. The work also dealt with finding some packaging that would not have a negative impact on the organism and generation of an innovative method of aluminium determination in antacids. The impact of aluminium salts on the concentration of chlorophylls and carotenoids in Sida Hermaphrodita L. was observed. The analysis focused on evaluation of presence and activity of plant defense enzymes – glucanases and chitinases using spectrophotometry and polyacrylamide gel electrophoresis.

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POSTER 8

Observation of potential genotoxic properties of aluminium ions

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Nowadays aluminium can be found almost everywhere. We can find aluminium containing raw materials in cosmetics, pharmaceuticals and other drug products or even in water we drink. Aluminium is often used as a pigment or thickening agent. However, recently aluminium has been linked to many disorders such as autism, Alzheimer disease, breast cancer or autoimmunity diseases. In our work we are trying to measure cytotoxicity of aluminium salts by MTT assay on mesenchyme stem cells derived from human adipose tissue. Subsequently potential genotoxicity of aluminium salts on the same cell line was determined by using Comet assay that enables to detect primary DNA damages (DNA breaks). Moreover, potential genotoxic activity of aluminium salts were established by DNA topology assay.

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