BCEXPOS: Breast Cancer and the Chemical, Nutritional and Social Exposome

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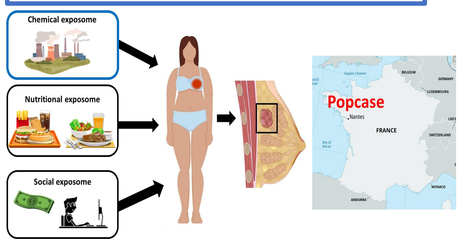
Background

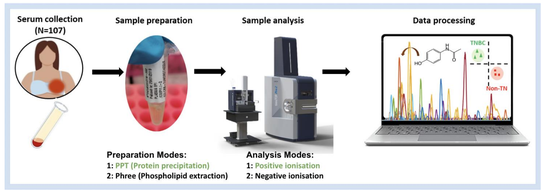
- Breast cancer is the most frequently diagnosed cancer in women worldwide and is a major cause of death for women in midlife
- Some risk factors of breast cancer are still unknown including those in the environment

Objective

- To map chemical, nutritional, and social exposures in one longitudinal cohort in Nantes, France
- To evaluate the association of these exposures and the incidence of triple negative breast cancer phenotype versus three less aggressive types of breast cancer
- To construct a logistic regression model which is controlled for multiple confounders

BCEXPOS Model





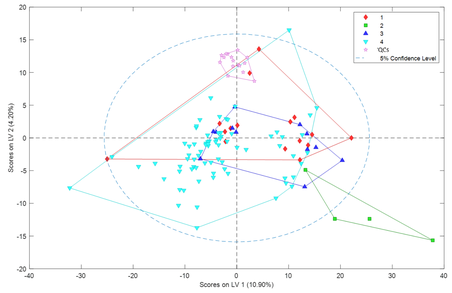
Methods

- Literature Review
  - Data base construction for the annotation (> 8000 molecules) with Pubchem
  - Literature research of chemicals in the database using google scholar tools
- Analysis of Cohort Data
  - Sample analysis by LC-MS/MS (liquid chromatography coupled to tandem mass spectrometry)
  - Feature detection, annotation, and quantification of annotated molecules with higher annotation quality (AQ) score with Metaboscape
  - Multivariate analysis for data visualization and evaluation of conformity
  - Univariate descriptive analysis of annotated pesticides with SAS and correlation matrix with Matlab
  - Multivariable analysis of variables related to TNBC with SAS

Results

Multivariate analysis for conformity evaluation

Phenotype 1: ER-PR-HER2- (Triple Negative)
Phenotype 2: ER-PR+HER2-
Phenotype 3: ER+PR-HER2-
Phenotype 4: ER+PR+HER2-

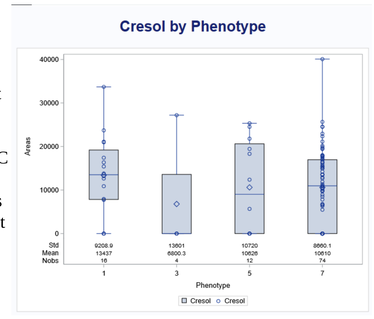


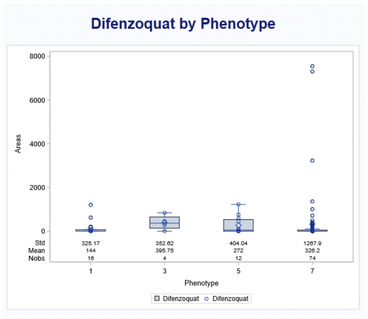
PLS-DA analysis was applied defining four classes (1-4 corresponding to different BC phenotypes) and QC (quality controls) representing the pool of samples. Six components were selected to build the model, explaining a cumulative Y-variance of 64.4%.

The small dispersion of quality control samples (pink spots) in contrast with the high dispersion of BC phenotypes, due to biological variability, indicates good robustness of sample preparation and analysis.

Unadjusted predictors of TNBC, n=106

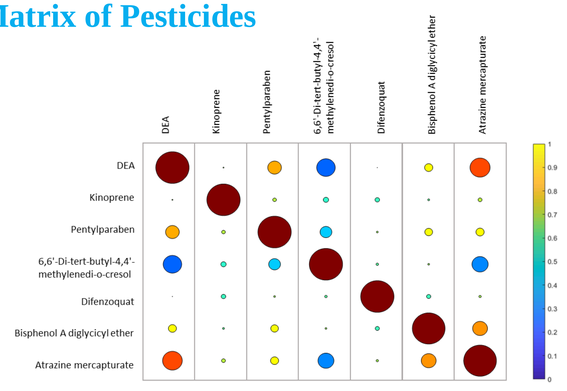
Among the four phenotypes, Cresol is present at the highest amount on average in TNBC phenotype compared to less aggressive breast cancer phenotypes





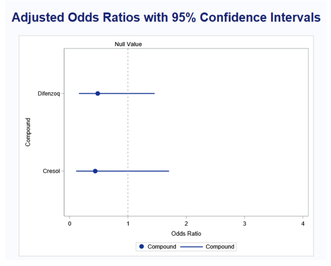
Among the four phenotypes, Difenzoquat is present at slightly higher amounts on average in less aggressive breast cancer phenotypes (phenotypes #2, 3, 4)

Correlation Matrix of Pesticides



Correlation between the two metabolites of the same pesticide, atrazine

Pesticide predictors of TNBC, n=106



Multivariable Logistic Regression						
	Non-Adjusted for Age and BMI			Adjusted for Age and BMI		
Compound	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-value
Cresol	2.167	(0.573, 8.190)	0.2544	0.439	(0.113, 1.705)	0.2344
Difenzoquat	1.727	(0.593, 5.034)	0.3166	0.482	(0.159, 1.458)	0.1962

Adjusted analyses showed individuals with Cresol and Difenzoquat exposure had decreased odds of having triple negative breast cancer phenotype than unexposed individuals.

Conclusion

Implications

- The detection of several pesticides with potential carcinogenicity was feasible by LC-MS/MS analysis of BC blood samples
- Data processing completed with bioinformatic tools shows that the variables BMI and age should be considered in future related studies

Next Steps

- Annotations are ongoing to include another mode of sample preparation and mode of ionization with a focus on pesticides
- Conduct a case control study with a new cohort
- Further work including variables such as relapse and smoking could enhance the model
- Expand the scope of analysis to include more chemicals

Competencies

Department

(1) Select among common epidemiologic study designs and explain their uses for solving epidemiological problems based on study goals and key sources of available data	Decided between case control and cohort study based on the data available
(2) Apply appropriate epidemiologic and statistical measures to generate, calculate, and draw valid inferences from public health data.	Calculated relevant epidemiological measures to analyze the data

Student Contributions

- Chemical database construction and annotation
- Literature research of chemicals in database
- Annotation of liquid chromatography- high resolution mass spectrometry
- Multivariate analysis for data visualization and evaluation of conformity
- Univariate descriptive analysis of annotated pesticides with SAS
- Multivariable analysis of determinant variables for triple negative breast cancer with SAS

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