

# MAY THE POST-TRANSLATIONAL PROCESS OF SUCCINATION BE INVOLVED IN CARDIAC ARRHYTHMIA?

A joint biological and chemical investigation

Afaf FIZAZI PhD student<sup>1,2</sup>, Laora SPINOZI, Vanessa TAGLIATTI<sup>1</sup>, Julien DE WINTER<sup>3</sup>, Anne-Emilie DECLEVES<sup>2</sup>, Jean-Marie COLET<sup>1</sup>.

<sup>1</sup>Human biology and toxicology laboratory, <sup>2</sup>Metabolic and Molecular Biochemistry Laboratory, <sup>3</sup>Organic Synthesis and Mass Spectrometry Laboratory (S<sup>2</sup>MOs), University of Mons. Mons, Belgium. A.R.C. Funding.

## Introduction

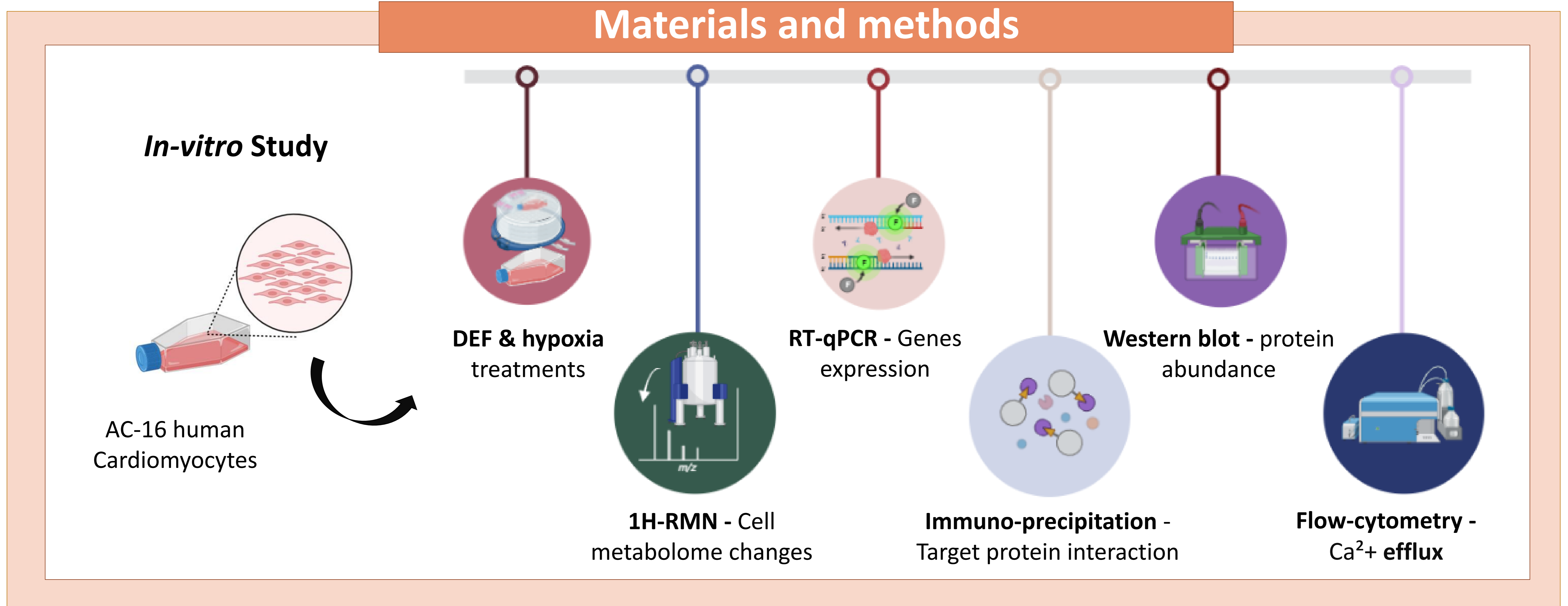
Small Ubiquitin Like Modifier 1 (SUMO1) is a protein that plays a key role in the regulation of calcium (Ca<sup>2+</sup>) homeostasis in heart cells. Indeed, SUMOylation of the sarcoplasmic/endoplasmic reticulum Ca<sup>2+</sup> ATPase 2a (SERCA2a) helps the reuptake of Ca<sup>2+</sup> after contraction.

Besides, some disorders in the cell can induce an increase of fumarate concentration. It has been proposed in the literature that free thiol from proteins can spontaneously react with fumarate, this reaction is called succination. SUMO1 bearing one free cysteine is then prone to such side reaction. In order to evaluate the spontaneity of this reaction, previous works in our lab were conducted in mass spectrometry. Indeed, this reaction of succination was confirmed to be spontaneous in buffered water at 37°C. Based on this significant result, it is hypothesized that the succination of SUMO1 might interfere with the SUMOylation of SERCA2a, hence interfering with its stability and its ATPase activity.

## Objectives

- Investigate the metabolome changes following exogenous and endogenous fumarate treatment.
- Study SUMO1/SERCA2a interaction before and after SUMO1 succination.
- Study the effects of SUMO1 succination on Ca<sup>2+</sup> efflux.

## Materials and methods

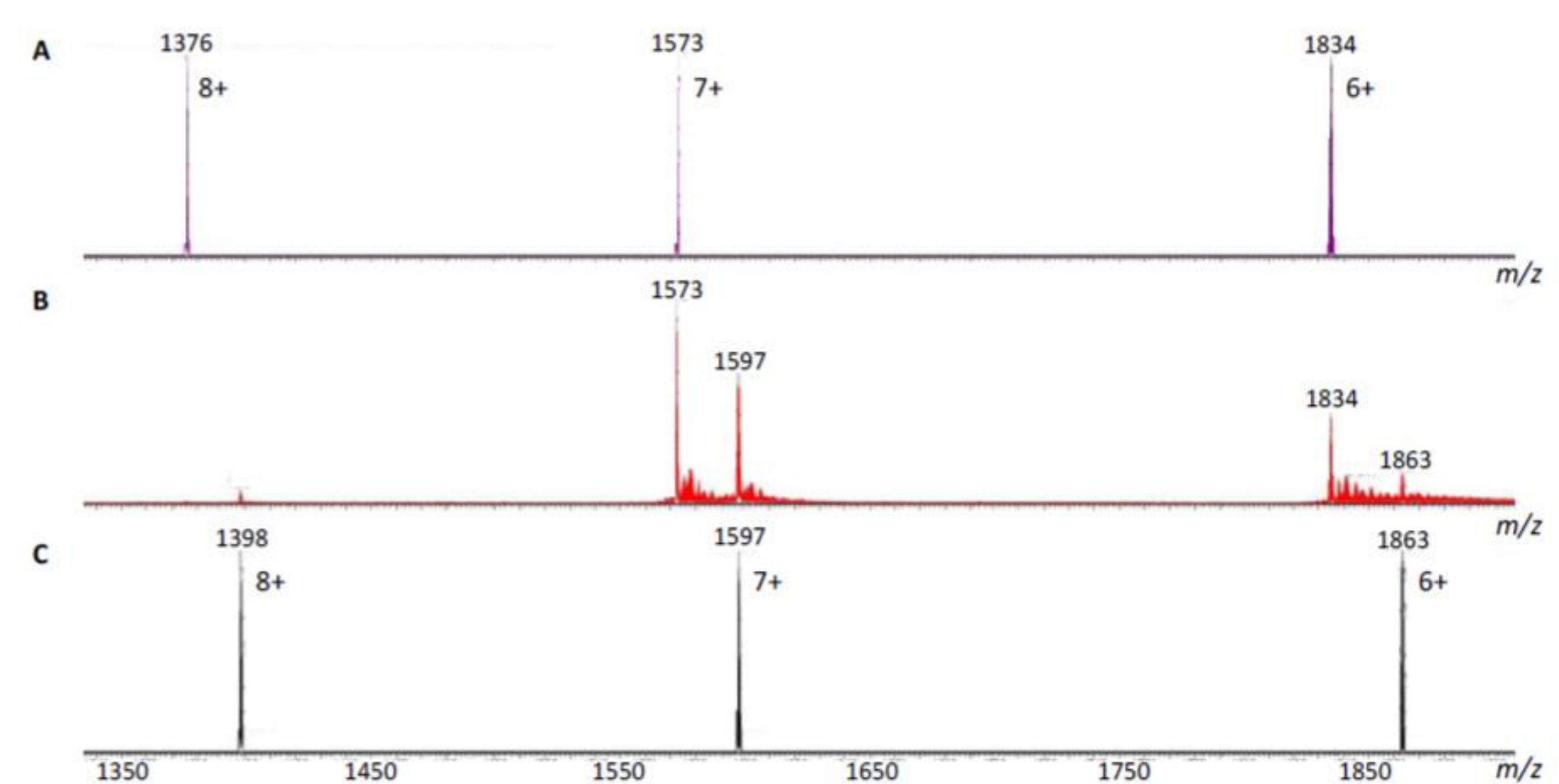


## Preliminary results

To study the spontaneity of the succination reaction, Electrospray Ionization mass spectrometry was used. In the context of this work, SUMO1 was characterized alone before analyzing the protein/fumarate solution. SUMO1 was mixed with diethyl fumarate in water for 24h at 37°C and different aliquots were withdrawn. The experimental spectra recorded for the solution was compared to theoretical distribution of succinated SUMO1. The appearance of new signal at higher mass to charge ratio (172 uma) confirmed the efficiency et spontaneity of the reaction.

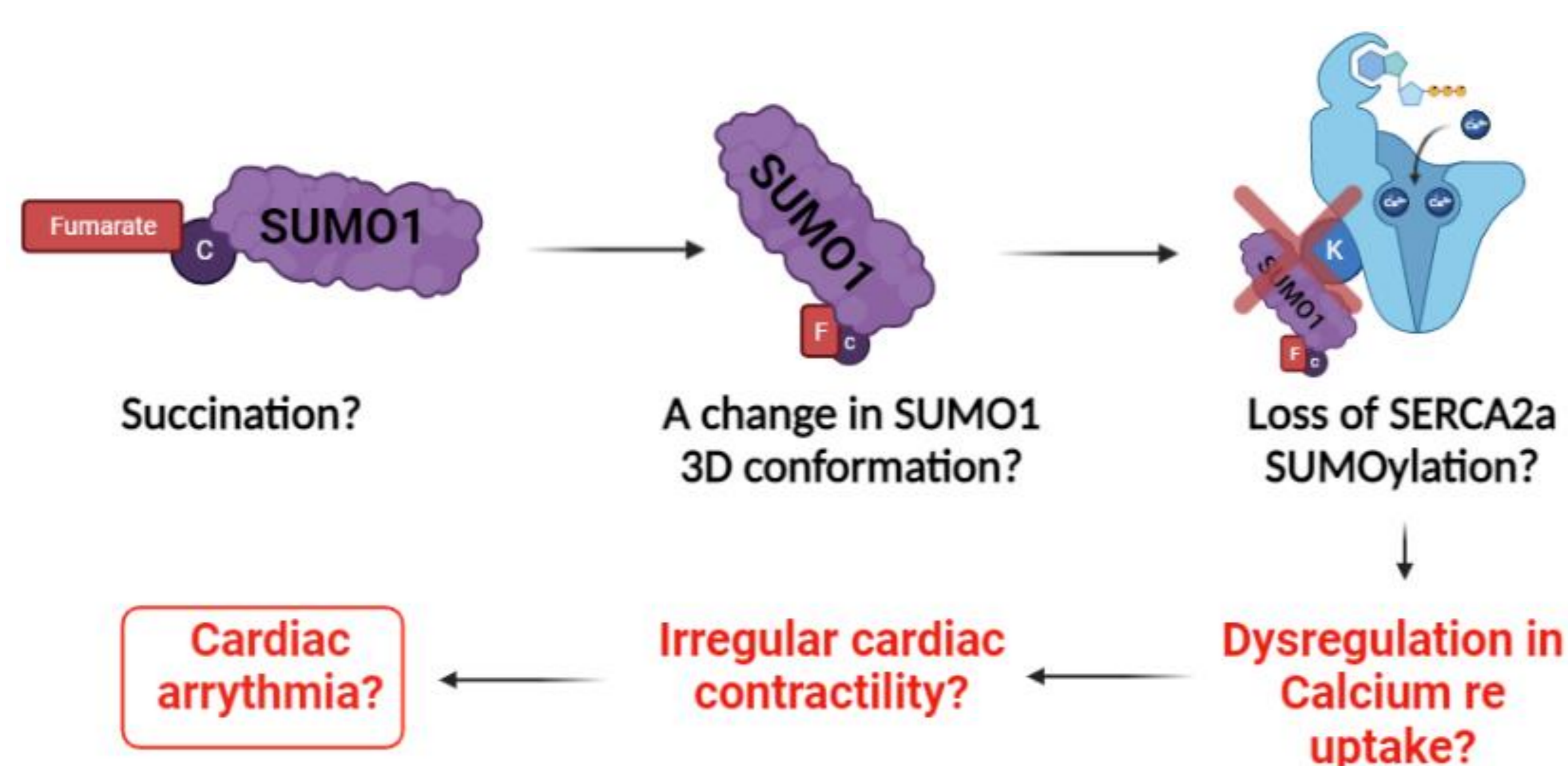
### Results:

- the tested models were in concordance with theoretical isotopic models
- SUMO1 is succinated by DEF
- The succination reaction is spontaneous



Electrospray mass analysis recorded on a Synapt G2-Si : A. Theoretical distribution of SUMO1 protein (C478H763N131O158S4), B. experimental spectrum of the SUMO1/DEF solution after 24hours of reaction, C. Theoretical distribution of succinated SUMO1 protein (C478H763N131O158S4C8H12O4). SPINOSI L. *et al.* (2021)

## Conclusion & prospects



## References

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