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ADPredict: ADP-ribosylation sites prediction based on physicochemical and structure descriptors

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Statement of the Problem: ADP-ribosylation is a post-translational modification governing several crucial cellular processes, such as inflammation, cell survival or damaged DNA detection and repairing machinery activation. It is, thus, strictly related to neoplastic conditions. To date, ADP-ribosylation is poorly understood, as still incomplete is the knowledge of its effects on numerous molecular paths. Deeply understanding the circumstances in which it happens, as well as the numerous target proteins and the way their role in their respective biological pathways are affected by this event, would represent an important achievement in molecular biology, not solely for the progression in combating cancer.

Methodology & Theoretical Orientation: *ADPredict* is an in silico predictive algorithm of ADP-ribosylated Aspartate and Glutamate residues, based on both known physicochemical parameters (Z-Scales, ST-Scales, MSWHIM, ProtFP) and in-house derived secondary structure related and 3-D descriptors of hundreds of human ribosylated proteins. ADPredict was developed using principal component analyses (PCA) and the random forest algorithm. Its predictive capacity was then evaluated via intensive boot-strap approaches.

Findings: Here we present the first computational predictive tool able to individuate the Aspartate or Glutamate residues that are most likely to be ADP-ribosylated in a target of interest. Predictions can be achieved via single or multiple models (meta-model strategy), so allowing each time a tailored approach. It will soon be available as an online service at the website www.Adpredict.net.

Conclusion & Significance: *ADPredict* arises as a new, concrete support to the study of the ADP-ribosylation event, flanking the analytic approaches developed so far and addressing the experimental investigation of this important biologic phenomenon. Ongoing extension of the predictive algorithm would aim to account also for the modification of additional amino acidic residues, so enlarging the applicability domain of the tool.

Recent Publications

1. Cilurzo F, Vistoli G, Selmin F, Gennari CG, Musazzi UM, Franzé S, Lo Monte M, Minghetti P (2014) An insight into the skin penetration enhancement mechanism of n-methylpyrrolidone. Mol Pharm 11(3):1014-1021.
2. Ostacolo C, Ambrosino P, Russo R, Lo Monte M, Soldovieri MV, Laneri S, Sacchi A, Vistoli G, Taglialatela M, Calignano A (2013) Isoxazole derivatives as potent transient receptor potential melastatin type 8 (TRPM8) agonists. Eur J Med Chem 69:659-69.
3. Pedretti A, Labozzetta A, Lo Monte M, Beccari AR, Moriconi A, Vistoli G (2011) Exploring the activation mechanism of TRPM8 channel by targeted MD simulations. BiochemBiophys Res Comm 414(1):14-19.

Biography

Matteo Lo Monte completed his PhD in Medicinal Chemistry with a project entitled, "*In silico* screening of taste receptors: An integrate modeling approach" in 2015, at the "Universita'degliStudi di Milano", under the supervision of Prof. Giulio Vistoli and in collaboration with Dompé Farmaceutici SpA, under Dr. Andrea Beccari. During this period, he mainly worked on the TRP receptors family, predicting their 3-D structure by homology modeling techniques and studying their interaction capacities as well as their activation mechanisms by Molecular Docking and Molecular Dynamic simulations; so generated models were conveniently utilized in virtual screening campaigns that successfully led to the identification of new hits. He moved to the Institute of Protein Biochemistry at the National Research Council in Naples in 2015 as Postdoctoral Fellow in the research group of Dr. Alberto Luini. He computationally supported several ongoing projects of Molecular Biology through molecular modeling and structural analyses studies of diverse enzymes like β4Galt5, SHIP1 and AGPAT4, as well as investigating the post-translational modifications, ADP-ribosylation in particular, developing predictive algorithms.

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