Identification of arginine methylation in colorectal cancer across the proteome.

Hanjie Chen*

Research Institute of Atherosclerotic Disease, Xi'an Jiaotong University Cardiovascular Research Centre, 710061, China

Abstract

Protein arginine methyltransferase (PRMT) catalyses the protein arginine methylation process, which is linked to several illnesses, including cancer. Currently, proteomics technique based on high-resolution mass spectrometry has been used to identify thousands of arginine methylation sites. It has not yet been documented how to identify arginine methylation using clinical samples at the proteome level. Finding monomethyl-arginine (MMA) and asymmetric dimethyl-arginine (ADMA) sites in colorectal cancer (CRC) tissues at the proteome level was the goal of the current investigation. Trypsin digestion of combined CRC tissue samples from 10 individuals with stage II and stage III was followed by additional processing and lyophilization. Methylarginine-containing peptides were isolated and then subjected to high-resolution LC-MS/MS analysis using monomethyl- or asymmetric dimethyl arginine (MMA or ADMA, respectively) motif kits. Colon cancer cells from DLD1 and HCT116 were treated with type I PRMTs inhibitor (MS023) alone or in combination with SN-38. The medicines' impact on CRC cell proliferation and apoptosis was assessed using the WST-1 test and FACS analysis, respectively.

Keywords: Proteome, Colorectal Cancer, Methyltransferase, Tissues.

Introduction

Numerous physiological processes, such as signal transduction, transcriptional control, RNA processing, and DNA repair, are affected by arginine methylation. Additionally, new research has linked protein arginine modification to the pathogenesis of a number of human disorders, including cancer. This suggests that improperly methylated proteins may serve as disease markers and that PRMTs may be useful as targets for future treatments. It became more crucial to identify arginine-methylated proteins and the sites of methylation residues within these proteins. Proteomics technology based on mass spectrometry (MS) has been widely used to identify arginine methylation across the proteome. Stable isotope labelling with amino acids in cell culture (SILAC) has been widely utilised to boost confidence in the identification of methylation sites and their relative measurement [1].

However, samples that are metabolically inactive, such as clinical tissues from patients, cannot be used with the SILAC approach. Recently, arginine-methylated peptide enrichment has been made achievable by the creation of highly selective antibodies against methyl-arginine. Numerous arginine-methylated sites from various biological sources have been found using immune-enrichment of arginine-methylated peptides and MS-based proteomics techniques. Additionally, site-specific quantitative characterisation of methylarginines between control and experimental groups may be possible using this approach. It is anticipated that high resolution MS coupled with effective enrichment strategies of arginine-methylated peptides will become increasingly valuable for both fundamental science and biomedical research as new enrichment procedures for arginine/lysine-methylated peptides have been developed. However, there hasn't yet been a publication on the proteome-wide detection of arginine methylation using clinical samples [2-3].

In the current study, we describe MMA and ADMA locations at the proteome level in CRC tissues from patients. We were able to locate hundreds of methylation sites, including a large number of unique MMA and ADMA sites, using immunoaffinity enrichment of methylated peptides in conjunction with LC-MS/MS techniques. This study's findings on arginine methylation sites and substrates for PRMTs were contrasted with data from the HCT116 colon cancer cell line. Finally, we looked into how SN, an active metabolite of irinotecan, interacted with type I PRMTs inhibitor to affect CRC cell growth and apoptosis [4].

We recently reported that quantitative study revealed that CRC tissue maintains a considerably greater level of symmetric arginine dimethylation compared to comparable noncancerous tissue. Several SDMA-containing proteins were overexpressed in CRC tissues compared to corresponding

***Correspondence to:** Hanjie chen, Research Institute of Atherosclerotic Disease, Xi'an Jiaotong University Cardiovascular Research Centre, 710061, China, Email: hanjiechen@gmail.com

***Received:** 02-Jan -2023, Manuscript No. AASBPR-23-87630; **Editor assigned:** 03-Jan-2023, PreQC No. AASBPR-23-87630(PQ); **Reviewed:** 17-Jan-2023, QC No. AASBPR-23-87630; **Revised:** 19-Jan-2023, Manuscript No. AASBPR-23-87630(R); **Published:** 24-Jan-2023, DOI: 10.35841/aasbpr-4.1.132*

***Citation:** Chen H. Identification of arginine methylation in colorectal cancer across the proteome. J Syst Bio Proteome Res. 2023;4(1):132*

noncancerous tissues, revealing that enhanced symmetric arginine modification in CRC tissues was primarily caused by overexpression of the substrate proteins. [5].

Conclusion

As far as we are aware, there has never been a report of high-throughput arginine methylation identification using clinical samples. The absence of acceptable methodologies has been a significant barrier. Recently, it has become possible to enrich each type of arginine-methylated peptide followed by high-resolution mass spectrometry analysis thanks to the discovery of highly specific antibodies against methyl-arginine in synthetic peptides. With the aid of these techniques, we discovered a total of arginine methylation sites that were present in distinct proteins of CRC tissues from patients. We also discovered fresh locations for arginine methylation and brand-new PRMT substrates. Our findings point to their important inclusion in protein complexes and RNA-binding proteins involved in transcription. Furthermore, CRC cells were markedly more sensitive to the chemotherapeutic drug SN-38 when treated with a powerful type I PRMT inhibitor. Our observations as a whole increase the number of in vivo arginine methylation sites known to exist and provide evidence that type I PRMTs could serve as potential therapeutic targets for the treatment of CRC.

References

1. Bedford MT, Richard S. Arginine methylation an emerging regulator of protein function. Mol Cell. 2005;18(3):263-72.
2. Paik WK, Paik DC, Kim S. Historical review: the field of protein methylation. Trends Biochem Sci. 2007;32(3):146-52.
3. Aletta JM, Hu JC. Protein arginine methylation in health and disease. Biotechnol Annu Rev. 2008;14:203-24.
4. Wei H, Mundade R, Langge KC, et al. Protein arginine methylation of non-histone proteins and its role in diseases. Cell Cycle. 2014;13(1):32-41.
5. Peng C, Wong CC. The story of protein arginine methylation: characterization, regulation, and function. Expert Rev Proteomics. 2017;14(2):157-70.

Citation: *Chen H. Identification of arginine methylation in colorectal cancer across the proteome. J Syst Bio Proteome Res. 2023;4(1):132*