Microreview of Multiple Myeloma

**Abstract**

As a blood cancer, Multiple Myeloma is a troubling illness that can compromise bone health and, in extreme cases, lead to death. A research experiment spearheaded by a team of doctors in 2013 revealed promising findings that could aid in the identification of the cause of this type of cancer. The invention of the PathSeq program might change scientists’ understanding of multiple myeloma and allow for more accurate disease testing in the future. Moreover this destructive cancer’s causation was successfully linked to viral infections in patients. This revolutionary discovery holds promise for unlocking more information about Multiple Myeloma, and could lead to a more thorough understanding of this cancer’s destructive nature and pathology.

**Introduction**

Multiple Myeloma is a concerning form of cancer. According to the Multiple Myeloma Research Foundation, Multiple Myeloma is a blood cancer that develops within the plasma cells of bone marrow.[[1]](#endnote-1) Bone marrow affected by this cancer will produce abnormal antibodies, most commonly in the form of M proteins. In an article detailing the issues related to Multiple Myeloma research, a team of scientists detailed the many discrepancies that are present in the research of this cancer. The inconsistencies in the research techniques used between various groups have made this cancer less than sufficiently documented in clinical cases. This group called for reform and increased emphasis on scientific consistency between different research projects relative to multiple myeloma.[[2]](#endnote-2)

Not only is multiple myeloma insufficiently documented, but also it holds high potential for destruction to the body.

The ultimate result of this cancer can be irreversible bone damage resulting from the interruption of the bone forming and bone breaking cells (osteoblasts and osteoclasts, respectively). Because of this interruption, bone cannot be properly reabsorbed which leads to the development of weaker bones. Hydroxyapatite, a crucial element of bones is bound after the onset of multiple myeloma and because osteoblasts cannot interact freely with these bound hydroxyapatite crystals the osteoclasts will be terminated. After the osteoblast cells are compromised, lesions or soft spots will develop within bones. These lesions and soft spots are often unable to support weight or to allow for proper locomotion and usually lead to bone fractures.[[3]](#endnote-3) Because of the role that bones play in immunity, a patient with advanced Multiple Myeloma could have such a weakened immune system that they could end up dying from an inability to fight off environmental pathogens.

**Discussion**

New information published in a report from the American Society of Hematology shed light onto infections that may be leading to multiple myeloma cancers. The group of scientists that conducted this research experiment hypothesized that there was a link between viral infections and the production of differentiated malignant B cells in bone marrow. According to the article, many previous researchers could have been mistaken when they were reviewing the role of prior infections as a factor that could lead to multiple myeloma. The researchers found that if careful attention is not paid when comparing human and pathogenic genetic material, then it could be difficult to acknowledge the presence of viral or bacterial material that might be intermingling with human DNA or RNA.[[4]](#endnote-4)

In order to address this potential complication, the research team used very intensive methods to collect data. The researchers utilized high-throughput sequencing, and computational subtraction of human sequence reads to in identify non-human, pathogenic sequences. This unique approach to unearthing new information relative to this cancer lead to new pools of knowledge becoming more accessible, and thus opened a door for subsequent researchers to be able to record more accurate information.[[5]](#endnote-5)

In order to study the sequences of pathogens more quickly, the team developed a “computational subtraction pipeline” that they dubbed PathSeq. PathSeq is composed of a pre-subtraction module, a subtraction module and a post-subtraction module. Each module plays a different role in the analysis and purification of sequence information. The pre-subtraction module is responsible for performing a quality filter. The subtraction module then analyzes the quality filtered reads of genetic information by aligning them through human genome and transcriptome technologies. In the post-subtraction step, the team aligned remaining, unaligned nucleotides and the translated sequences using microbe alignment programs. In this step the team thoroughly analyzed some of the unmapped genetic material that was retrieved from the sample. Because this genetic material was unable to be annealed and read it was presumed that this material lacked alignment similarity to that present in the sequence reference programs. In other words, this material was likely donated by a pathogen.[[6]](#endnote-6)

 In order to test this newly developed technology further, genomic data from 26 myeloma tumor samples were analyzed using PathSeq. Results from this testing revealed the Epstein-Barr virus sequence was present in 7 specimens. Additionally, the human herpes virus 6B was present in 2 more specimens. The 7 sample sequences that contained Epstein-Barr genetic information were compared to 13 tumors that lacked viral sequences, but still showed signs of a viral infection. These 13 tumors, while lacking viral sequences, did test positive for SHISA2, which is a gene commonly expressed by viruses.[[7]](#endnote-7) The presence of these traces from viral infections in patients afflicted with Multiple Myeloma proved to be one of the newest breakthroughs that could be directly attributed to the development of the PathSeq technologies. The new methods of DNA researching using this technology allowed for scientists to acknowledge the role that viral infections could be playing in setting the stage for the onset of Multiple Myeloma. This breakthrough will allow for scientists to follow the events that could lead up to the development of the cancerous bone formations we know as Multiple Myeloma.

**Conclusions**

The American Cancer Society estimates that annually there are 30,330 individuals diagnosed with Multiple Myeloma, and of those diagnosed, about 12,650 individuals die from this form of cancer on a yearly basis.[[8]](#endnote-8) The emergence of the PathSeq technologies has shown promise for highlighting the connection between multiple myeloma and previous viral infections. While this data needs to be supported by further studies, it was able to refine the methodology of gathering information in research. Time will likely aid in the perfection of this science and it can be used in future testing for multiple myeloma, testing that could help save lives. By uniting researchers and gaining more uniform data collection techniques the PathSeq has emerged as a frontrunner in the race to gain more knowledge about Multiple Myeloma.

# References

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