

## Supplementary Online Content

Landgren O, Rachel Zeig-Owens R, Giricz O, et al. Multiple myeloma and its precursor disease among firefighters exposed to the World Trade Center disaster. *JAMA Oncol*. Published online April 26, 2018. doi:10.1001/jamaoncol.2018.0509

**eTable 1.** Post-9/11 multiple myeloma cases among WTC-exposed FDNY white male firefighters

**eTable 2.** Myeloma precursor disease screening study: characteristics of MGUS and light-chain-MGUS in WTC-exposed FDNY white male firefighters

This supplementary material has been provided by the authors to give readers additional information about their work.

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**eTable 1. Post-9/11 multiple myeloma cases among WTC-exposed FDNY white male firefighters**

| <b>Patient number</b> | <b>Age at diagnosis</b> | <b>Plasma cell % in the bone marrow</b> | <b>Serum/urine monoclonal protein isotype and free light-chains</b> | <b>CD20 expression on plasma cells</b> |
|-----------------------|-------------------------|---|---|--|
| 1                     | 58                      | 40-50%                                  | —*  | Positive                               |
| 2                     | 59                      | 10%                                     | Free lambda light-chain   | Positive                               |
| 3                     | 38                      | —*                                      | Free lambda light-chain   | ND                                     |
| 4                     | 55                      | >15%                                    | Free lambda light-chain   | Negative                               |
| 5                     | 65                      | 50%                                     | Free kappa light-chain  | ND                                     |
| 6                     | 46                      | 80-90%                                  | IgG lambda & free lambda light-chain                                | Negative                               |
| 7                     | 56                      | 20%                                     | IgG kappa & free kappa light-chain                                  | ND                                     |
| 8                     | 74                      | 80-90%                                  | Free lambda light-chain   | ND                                     |
| 9                     | 49                      | 10%                                     | IgG kappa & free kappa light-chain                                  | ND                                     |
| 10                    | 46                      | —*                                      | —*  | ND                                     |
| 11                    | 52                      | 25%                                     | IgG kappa   | Positive                               |
| 12                    | 52                      | —*                                      | Free kappa light-chain  | ND                                     |
| 13                    | 71                      | 60-70%                                  | IgG lambda & free lambda light-chain                                | Positive                               |
| 14                    | 60                      | 80-90%                                  | IgG lambda & free lambda light-chain                                | ND                                     |
| 15                    | 69                      | >10%                                    | IgG lambda & free lambda light-chain                                | Positive                               |
| 16                    | 76                      | <10%**                                  | Free kappa light-chain  | ND                                     |

**Footnote:** The WTC Health Program provide comprehensive physical and mental health services to WTC exposed. All responders from the FDNY databases with a post-9/11 diagnosis of multiple myeloma are included in the above case series population (until 7/1/2017). The information was obtained through review of medical records from the time of diagnosis.

**Abbreviations:** ND = not done; -\* = data missing; \*\*Extramedullary plasmacytoma, plasma cell percentage in the bone marrow <10%

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**eTable 2. Myeloma precursor disease screening study: characteristics of MGUS and light-chain-MGUS in WTC-exposed FDNY white male firefighters**

| Characteristic of MGUS                     | WTC- exposed FDNY firefighters,<br>(n=781) |           |
|--|--|-----------|
|  | n  | %         |
| MGUS                                       |  |           |
| Overall MGUS <sup>a</sup>                  | 47   | 6.01      |
| MGUS                                       | 29   | 3.71      |
| IgG  | 17   | 2.18      |
| IgA  | 6  | 0.77      |
| IgM  | 5  | 0.64      |
| Biclonal <sup>b</sup>                      | 1  | 0.13      |
| Light-chain-MGUS                           | 18   | 2.30      |
| <b>Concentration, Median (IQR)</b>         |  |           |
| M-protein g/dL <sup>c</sup>                | 0.37                                       | 0.21-0.59 |
| Free-κ light chain, mg/dL <sup>d</sup>     | 2.32                                       | 2.12-2.74 |
| Free-λ light chain, mg/dL <sup>d</sup>     | 1.23                                       | 1.09-1.38 |
| dFLC, mg/dL <sup>d</sup>                   | 1.15                                       | 0.95-1.65 |
| <b>FLC-ratio, median (IQR)<sup>d</sup></b> | 1.86                                       | 1.70-2.19 |

Abbreviations:

dFLC: difference between involved and uninvolved free light chains

FLC: free light chain

IQR: Interquartile Range

MGUS: monoclonal gammopathy of undetermined significance

<sup>a-</sup> Includes MGUS and light-chain-MGUS cases

<sup>b-</sup> One firefighter had 2 separate bands of IgG

<sup>c-</sup> Based on 29 firefighters whose M-protein concentration was quantifiable

<sup>d-</sup> Based on 18 firefighters who had light-chain-MGUS as described in the methods section

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Footnote: To rule out MGUS and light-chain-MGUS, all serum specimens were first analyzed using conventional agarose-gel electrophoresis to determine the occurrence and pattern of M-protein bands, as described previously.<sup>17</sup> Samples observed with an M-protein band, equivocal band pattern, or abnormal free light-chain-(FLC)-ratio, were further analyzed by immunofixation to characterize the heavy- and light-chain isotypes of the M protein. Serum protein electrophoresis and immunofixation were performed using the SPIFE 3000 (Helena Laboratories). The FLC levels in all serum specimens were determined using a turbidimetric assay (Freelite; The Binding Site) performed on a SPAPLUS Automated Analyzer for Specialist Protein Analysis.<sup>16</sup> The Freelite assay (also used for the Olmsted County study that served as our external control) comprises 2 separate measurements: one to detect free- $\kappa$  light chains (normal range, 3.3-19.4 mg/L), and the other to detect free- $\lambda$  light chains (normal range, 5.7-26.3 mg/L).<sup>15</sup> We assessed monoclonality based on the  $\kappa/\lambda$  FLC-ratios.<sup>16</sup> MGUS cases were defined as having M-protein bands on SPEP and an M-protein concentration less than 30g/L.<sup>5</sup> Light-chain-MGUS was defined as the presence of an FLC band without heavy-chain expression in immunofixation or presence of an abnormal FLC-ratio (normal reference: 0.26-1.65) with an increased level (above the upper limit of normal) of the involved light chain.<sup>5,15</sup>

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