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TITLE: Inflammation as a Driver of Clonal Evolution in Myeloproliferative Neoplasm

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14. ABSTRACT Tumor Necrosis Factor-alpha (TNF) is elevated in myeloproliferative neoplasm (MPN) and plays a key role in expansion of the <i>JAK2</i> ^{V617F} neoplastic clone. We have found that MPN monocytes produce excessive amounts of TNF in response to TLR ligation due to a defect in the negative regulatory feedback loop which normally serves to dampen TNF production. We have localized this defect to a blunted response to the anti-inflammatory cytokine IL-10. MPN monocytes are less responsive to the anti-inflammatory actions of IL-10 at low concentrations but these effects can be restored by increasing the concentration of IL-10. Together, these data suggest that administration of IL-10 may reduce excessive inflammatory cytokine production in MPN.					
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Table of Contents

	<u>Page</u>
1. Introduction.....	3-4
2. Keywords.....	4
3. Accomplishments.....	4-12
4. Impact.....	13-14
5. Changes/Problems.....	14
6. Products.....	15-18
7. Participants & Other Collaborating Organizations.....	18-21
8. Special Reporting Requirements.....	21
9. Appendices.....	22

1. Introduction

Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Excessive production of inflammatory cytokines such as TNF is a characteristic feature of MPN. Excessive inflammation is not only responsible for the debilitating constitutional symptoms associated with this disease but also plays a central role in MPN disease initiation and progression. However, the mechanism causing excessive inflammation in MPN is not known. As a potential consequence of this gap in knowledge, MPN patients have no pharmacologic therapeutic options that alter the natural history of their disease. In order to accurately target harmful inflammation in MPN while preserving critical anti-inflammatory pathways, we must first define the mechanism driving excessive inflammation in MPN. The overall objectives of this project are to define the mechanism driving excessive TNF production in MPN and to identify agents that have the ability to dampen TNF production in MPN for further development as therapeutics.

2. Keywords

Myeloproliferative neoplasm, JAK2V617F, IL-10, inflammation, TNF, TLR signaling

3. Accomplishments

The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

- **What were the major goals of the project?**
 - *List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project identify these dates and show actual completion dates or the percentage of completion.*

The major goals of this project are to define the mechanism causing excessive TNF production in MPN patients, to identify the role of JAK2V617F in abnormal TLR signaling, and to restore the TLR negative feedback loop as a therapeutic approach in MPN.

- **What was accomplished under these goals?**
 - *For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.*

MPN patients produce more TNF- α in response to the TLR agonists

We measured TNF- α production by CD14⁺ monocytes stimulated with the TLR agonists LPS (TLR4) and R848 (TLR7/8), comparing MPN patients and normal controls (Figure 1A). CD14⁺

cells were purified from fresh peripheral blood and incubated for 24 hours in the presence of increasing concentrations of TLR agonists. The concentration of TNF- α in the supernatant of MPN patient monocytes was higher than that of normal controls in response to both LPS and R848 ($p \leq 0.05$).

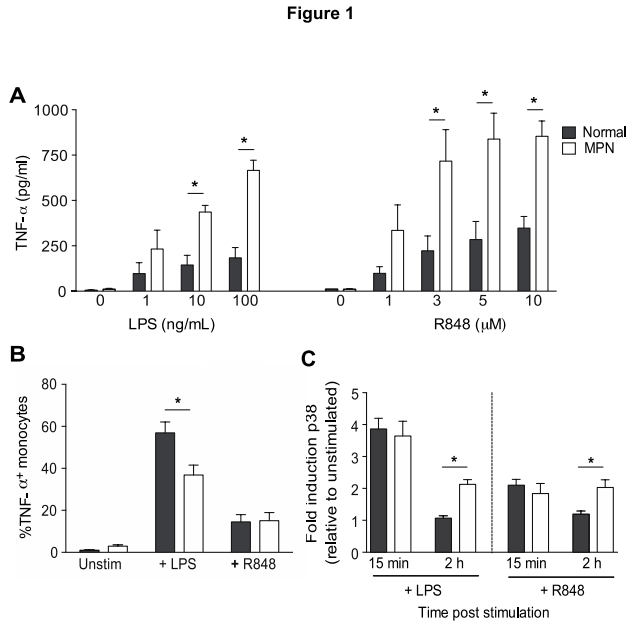


Figure 1. Increased TNF- α production by MPN monocytes following stimulation with TLR agonists. (A) MPN (n=5) and normal (n=5) monocytes were stimulated with TLR agonists LPS or R848 at the concentrations shown. After 24 hours of culture, supernatant was harvested and TNF- α was measured by ELISA. (B) MPN (n=13) and normal (n=8) monocytes were stimulated with 10ng/mL LPS or 5 μ M R848 and incubated with brefeldin-A for 4 hours to prevent protein export. Intracellular staining for TNF- α was performed and cells were analyzed by flow cytometry. (C) MPN (n=7) and normal (n=5) monocytes were stimulated with 10ng/mL LPS or 5 μ M R848 for 15 minutes or 2 hours prior to fixation and permeabilization. Cells were stained for phospho-p38 and analyzed on a flow cytometer.

Next, we compared the fraction of CD14⁺ monocytes that were actively producing TNF- α immediately after TLR ligation in MPN patients versus normal controls. We stimulated MPN and normal control peripheral blood mononuclear cells with the LPS or R848 for four hours along with brefeldin A (BFA) to retain TNF- α inside the cell and then used intracellular flow cytometry to quantify the percentage of CD14⁺ monocytes that were TNF- α^+ (Figure 1B). In unstimulated and R848-stimulated cells, there was no difference in the percentage of TNF- α^+ CD14⁺ monocytes in MPN and normal controls ($p > 0.05$). Surprisingly, normal controls had a higher fraction of TNF- α^+ cells than MPN patients following LPS stimulation ($p = 0.0001$). We also measured TNF- α production using ELISA at early time points (4hrs) following LPS stimulation by and found no difference in the amount of TNF- α produced by MPN versus normal controls (data not shown). Furthermore, MPN patients and normal controls have a similar fraction of CD14⁺CD16⁺ proinflammatory monocytes (data not shown). Thus, the increased TNF- α production in response to TLR ligation cannot be explained by an increased fraction of monocytes actively producing TNF- α immediately after stimulation but instead may be due to persistent TNF- α production at later time points post stimulation.

Sustained activation of TLR signaling pathway in MPN monocytes

The mitogen activated protein kinase (MAPK) pathways are key signaling intermediates in the cellular response to TLR stimulation. Activation of p38 MAPK is necessary for production of

TNF- α following LPS stimulation¹. Therefore, we next quantified induction of phosphorylated p38 MAPK in CD14⁺ monocytes from MPN versus normal controls 15 minutes and 2 hours after stimulation with LPS and R848 using phosphoflow (Figure 1C). At 15 minutes both LPS and R848 induced an equivalent fold induction of phospho-p38 in MPN and normal controls, demonstrating that initial signaling following TLR stimulation is not exaggerated in MPN. At two hours after stimulation with LPS and R848, however, phosphorylation of p38 was maintained or even increased in MPN patients, whereas at two hours after stimulation phosphorylation of p38 returned to baseline in normal controls. These data suggest that failure to dampen TLR signaling may be responsible for the persistent TNF- α production following TLR stimulation in MPN.

Persistent production of TNF- α by MPN patient monocytes following TLR ligation

We next compared the tempo of TNF- α production in MPN versus normal controls following TLR stimulation. We stimulated monocytes with LPS and quantified TNF- α in the supernatant at 4, 9, 18, and 24 hours later. The concentration of TNF- α at 4 hours was normalized to 1 for each patient to more easily visualize changes over time. In normal controls the concentration of TNF- α was greatest at 4 hours then consistently declined over time, but in MPN patients the concentration of TNF increased over time, peaking at 18 hours post-LPS and persisted even at 24 hours post-LPS (Figure 2A). We also performed intracellular flow cytometry at multiple time points following LPS stimulation and found that monocytes from MPN patients maintained a higher percentage of TNF- α ⁺ monocytes at later time points as compared to normal controls (Figure 2B). Our observations that the exaggerated TNF- α production is seen at late but not early time points following LPS stimulation implicates a defect in the TLR signaling negative feedback loop in MPN patients.

Blunted response to IL-10 by MPN monocytes is responsible for persistent TNF- α production in response to TLR ligation

IL-10 is produced in monocytes in response to LPS stimulation and acts as a negative-feedback mechanism to dampen TNF- α production². To test the hypothesis that MPN monocytes produce less IL-10 in response to TLR activation, we measured IL-10 production by ELISA in MPN and

Figure 2

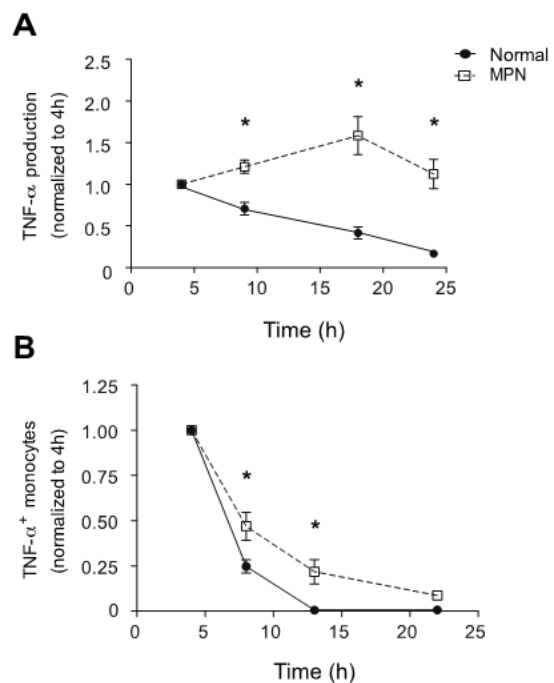


Figure 2. MPN monocytes persistently produce high level of TNF- α . (A) MPN (n=16) and normal (n=13) monocytes were stimulated with 10ng/ml of LPS for 4, 9, 18, 24h before harvesting supernatant for ELISA. The amount of TNF- α produced at 4h was normalized to 1. (B) MPN (n=11) and normal (n=6) monocytes were stimulated with 10ng/ml LPS for 4h, 8h, 13h, and 22h before harvesting for flow cytometry analysis. All samples were treated with brefeldin-A for 4h before harvesting. The percent of monocytes expressing TNF- α at 4h was normalized to 1.

normal control monocytes. We found that MPN monocytes produce at least as much IL-10 as normal controls at all time points after LPS-stimulation (Figure 3A). These data demonstrate that MPN patient monocytes produce adequate IL-10 in response to TLR stimulation and yet do not dampen TNF- α production.

We then measured the ability of recombinant human IL-10 (rhIL-10) to dampen LPS induced TNF- α production in MPN patients and normal controls. A low concentration (0.5ng/mL) of recombinant human IL-10 reduced LPS-induced TNF- α production by monocytes (Figure 3B) as well as the percentage of TNF- α ⁺ monocytes (Figure 3C) by greater than 50% in normal controls but only by 25% in MPN patients. However, higher concentrations of IL-10 (5, 10ng/mL) were able to reduce LPS-induced TNF- α production in normal and MPN monocytes to a similar degree. This suggests either that IL-10 produced by MPN monocytes is inherently ineffective or that IL-10R signaling in MPN patient monocytes is blunted in MPN compared to normal controls.

Figure 3

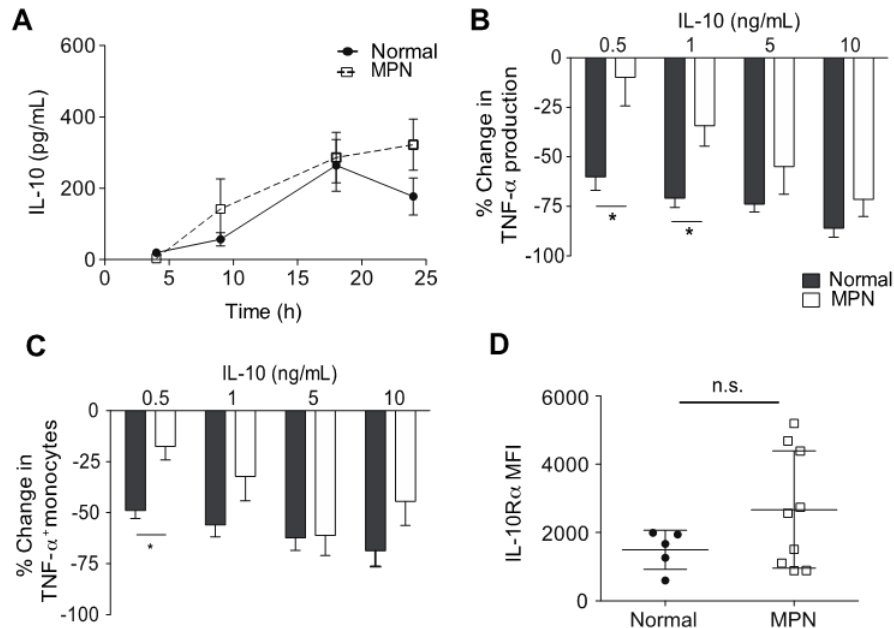


Figure 3. MPN monocytes produce adequate IL-10 but are less responsive to IL-10. (A) MPN (n=11) and normal (n=7) monocytes were stimulated with 10ng/ml of LPS for 4, 9, 18, 24h before harvesting supernatant for quantification of IL-10 via ELISA. (B) MPN (n=6) and normal (n=6) monocytes were stimulated with 10ng/ml of LPS and various concentration of IL-10 simultaneously for 4 hours between harvesting of the supernatant for ELISA. The percent change in TNF- α is measured by the difference in TNF- α production between adding IL-10 and without IL-10. (C) MPN (n=5) and normal (n=5) monocytes were stimulated with 10ng/ml of LPS and various concentration of IL-10 for 4 hours with brefeldin-A before performing intracellular staining for TNF- α . The change in TNF- α positive monocytes are measured by the difference in monocytes expressing TNF- α between adding IL-10 and without IL-10. (D) The mean fluorescence intensity (MFI) of IL-10 receptor α is measured by gating on MPN (n= 9) and normal (n=5) CD33^{high} CD14⁺ monocytes from mononuclear cells using flow cytometry analysis.

We measured IL-10R (CD210) cell surface expression in MPN and normal control monocytes by flow cytometry and did not find a decrease in IL-10R expression in MPN patients (Figure 3D). To further evaluate IL-10R signaling in MPN patients, we compared phospho-STAT3 (pSTAT3) activation of MPN versus normal control monocytes in response to IL-10 stimulation (Figure 4A). MPN monocytes did not induce pSTAT3 as robustly as normal controls in response to 10ng/mL or 50ng/mL IL-10 ($p \leq 0.01$). Because SOCS3 expression is typically upregulated in response to IL-10R activation and dampens cytokine signaling,^{3,4} we also compared mRNA levels of SOCS3 in MPN versus normal control monocytes stimulated with IL-10 (Figure 4B). IL-10 at high concentrations did not induce expression of the SOCS3 gene as effectively in monocytes of MPN patients as it did in normal controls. Taken together, our observations demonstrate that MPN monocytes have blunted IL-10R signaling resulting in unrestrained TLR-agonist-induced TNF- α production.

Figure 4

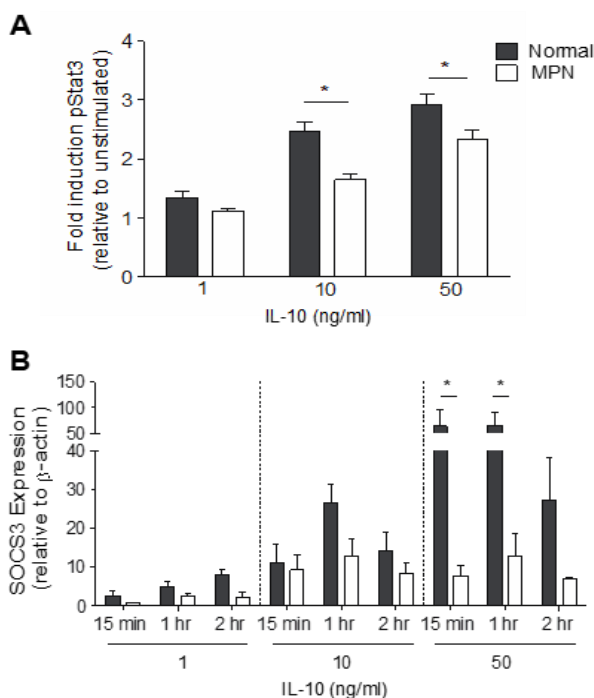


Figure 4. MPN monocytes have defective IL-10 signaling. (A) MPN (n=19) and normal (n=18) peripheral blood were stimulated for 15 minutes with IL-10 at the concentrations shown prior to fixation and permeabilization. CD33^{high} Cd14⁺ monocytes were gated for pStat3 and analyzed via flow cytometry. (B) MPN (n= 3) and normal (n=3) monocytes were stimulated with IL-10 for 15 min, 1h, or 2h at the concentrations shown. SOCS3 mRNA was quantified by qPCR and normalized to β -actin.

Blockade of IL-10R signaling induces persistent TNF- α production in normal control monocytes

We inhibited IL-10R signaling in normal control monocytes using an IL-10R blocking antibody and measured the impact on LPS induced TNF- α production over time (Figure 5A). Whereas IL-10R blockade did not have an impact on LPS induced TNF- α production at early time points (4hrs) IL-10R blockade increased LPS induced TNF- α production at later time points, confirming our expectation that blocking IL-10R in normal monocytes should induce them to produce TNF with MPN-like kinetics.

IL-10 resistance correlates with TNF- α persistence in MPN patients

We found that the degree of TNF- α persistence following LPS stimulation as well as the ability of IL-10 to dampen LPS induced TNF- α production was variable among MPN patients, with some patients being extremely abnormal and others being closer to normal. We reasoned that if TNF- α persistence is due to blunted IL-10R signaling then those patients with less of an ability to respond to IL-10 should have more extreme TNF- α persistence. For each MPN patient and normal control we calculated the “TNF- α persistence score”, defined as ([TNF- α at 24hrs]/[TNF- α at 4hrs]) as well as the “IL-10 resistance score”, defined as ([TNF- α of LPS + 1ng/mL IL-10]/[TNF- α of LPS + 0ng/mL IL-10]) (Figure 5B). We found that the TNF- α persistence score and the IL-10 resistance score had a Pearson correlation coefficient (r) of 0.72, demonstrating that the inability of IL-10 to reduce LPS induced TNF- α production correlates with an increased amount of TNF- α at 24 hours as compared to 4 hours as would be expected if IL-10 resistance is responsible for the persistent TNF- α production in MPN patients.

Figure 5

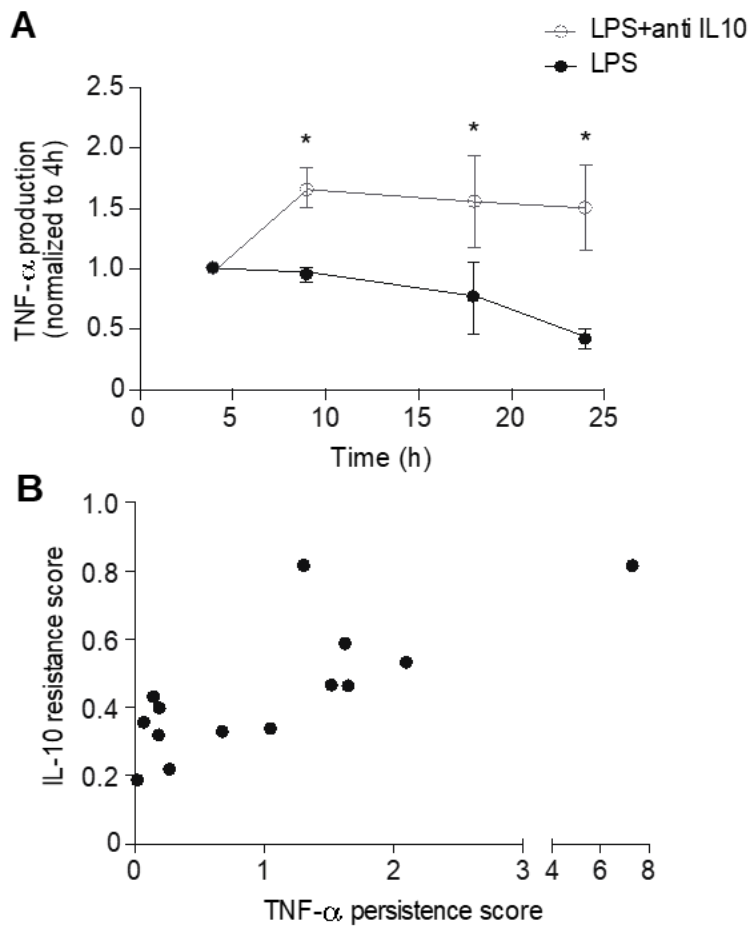


Figure 5. IL-10R blocking is correlated to elevated TNF- α .

(A) Normal monocytes (n=3) were stimulated with 10ng/ml of LPS and with the addition of 1 μ g/ml of anti IL-10R. Supernatants were collected for TNF- α quantification by ELISA at 4, 9, 18 and 24h after LPS stimulation. The amount of TNF- α produced at 4h was normalized to 1. (B) The correlation of TNF- α persistence score in MPN monocytes (n=14) is defined as [TNF- α at 24hrs]/[TNF- α at 4hrs] and IL-10 resistance score is defined as [TNF- α of LPS + 1ng/mL IL-10]/[TNF- α of LPS + 0ng/mL IL-10]. Pearson r = 0.7198, R² = 0.5181.

Persistent TNF- α production is a feature of both wild-type and $JAK2^{V617F}$ monocytes from $JAK2^{V617F}$ -positive patients

To determine whether the persistent TNF- α production following TLR ligation is driven by $JAK2^{V617F}$, we sorted TNF- α^+ and TNF- α^- CD14 $^+$ monocytes from $JAK2^{V617F}$ -positive MPN patients at 4 and 10 hours post LPS stimulation and quantified the $JAK2^{V617F}$ allele burden in each population (Table 1). We reasoned that if persistent TNF- α was driven by $JAK2^{V617F}$ in a cell intrinsic manner then the $JAK2^{V617F}$ allele burden should be higher in the sorted TNF- α^+ population as compared to the sorted TNF- α^- population at 10 hours post LPS stimulation (data not shown). We found the $JAK2^{V617F}$ allele burden was similar in the TNF- α^+ and TNF- α^- fractions both at 4 and 10 hours post stimulation, demonstrating that the both wild-type and $JAK2^{V617F}$ mutant monocytes from MPN patients contribute to the persistent TNF- α production in MPN patients. This suggests that $JAK2^{V617F}$ does not drive persistent TNF- α production following LPS stimulation in a cell autonomous manner. Instead, $JAK2^{V617F}$ mutant cells may induce this phenotype upon neighboring cells or alternatively unrestrained TLR-agonist-induced TNF- α production could be an intrinsic feature of MPN patients and could potentially be a predisposing factor to acquire the disease.

Table 1: Allele burden (% $Jak2^{V617F}$)

Patient	4 hr		10 hr	
	TNF- α^-	TNF- α^+	TNF- α^-	TNF- α^+
192	92.21	57.52	85.58	82.65
228	63.66	57.92	90.01	78.10
232	34.88	42.66	53.13	51.90
252	94.84	90.50	66.20	63.45
255	20.95	76.86	75.24	80.23

Table 1. $JAK2^{V617F}$ allele burden in TNF- α^+ monocytes. MPN monocytes (n=5) were stimulated with 10ng/mL LPS for 4 or 10h in the presence of BFA and intracellularly stained for TNF- α . TNF- α^+ cells were sorted and $JAK2^{V617F}$ allele burden was determined by quantitative PCR.

Expression of $JAK2^{V617F}$ does not induce persistent TNF- α production following TLR ligation

Next, we used $Jak2^{V617F}$ knock-in mice⁵ to more specifically test whether $JAK2^{V617F}$ induces persistent production of TNF- α following TLR stimulation. We isolated bone marrow-derived macrophages (BMDM) from normal and $Jak2^{V617F}$ knock-in mice and stimulated them with LPS. Intracellular cytokine staining demonstrated that $Jak2^{V617F}$ knock-in macrophages do not produce TNF- α longer than wild-type macrophages in response to LPS stimulation (data not shown). Therefore, the results of our murine studies provide additional support for the notion that the TNF- α production following TLR ligation we observe in MPN patients is not directly driven by $JAK2^{V617F}$ but instead is a unique feature of MPN patients.

Persistent TNF- α production following TLR ligation in an unaffected identical twin of MPN patient

We obtained monocytes from identical twins, discordant for MPN. One had $JAK2^{V617F}$ positive Polycythemia Vera (PV) and the other had no evidence of an MPN (normal blood counts, no detectable $JAK2^{V617F}$, $CALR$, or MPL mutant cells by NGS sequencing). We stimulated monocytes from each twin and two age and sex matched normal control with LPS and measured TNF- α and IL-10 production over time by ELISA. We found that both the PV patient and her unaffected twin had prolonged production of both TNF- α and IL-10 as compared to the normal control (Figure 7A and Figure 7B). We also observed that monocytes of the unaffected twin were less able to dampen LPS induced TNF- α production in response to IL-10 (Figure 7C) than were normal monocytes. The conservation of prolonged TLR agonist-induced TNF- α production as well as blunted IL-10 response in both the PV patient and her unaffected identical twin suggests that this abnormality predates the development of MPN and is not a consequence of the $JAK2^{V617F}$ mutation. That is, the aberrant monocyte response may be an intrinsic feature of those predisposed to acquire MPN.

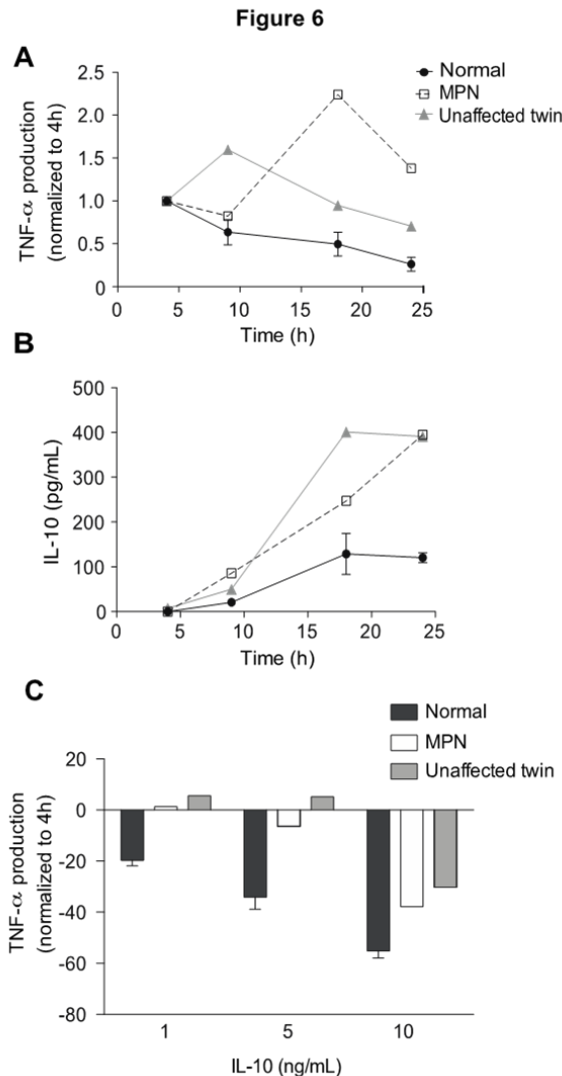


Figure 6. Persistent TNF- α production and IL-10R signaling defects are found in an unaffected twin of MPN patient. (A) The monocytes of a MPN patient, the unaffected twin of the patient, and normal donors (n=2) were stimulated with 10ng/ml of LPS for 4,9,18, and 24h before supernatants were harvested for ELISA. The amount of TNF- α produced at 4h was normalized to 1. (B) The same supernatants harvested in A were taken for quantifying IL-10. (C) The monocytes of a MPN patient, the unaffected twin of the patient, and normal donors (n=2) were stimulated with 10ng/ml of LPS and various concentration of IL-10 simultaneously for 4 hours between harvesting of the supernatant for TNF- α ELISA. The percent change in TNF- α is measured by the difference in TNF- α production between adding IL-10 and without IL-10.

References:

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2. Siewe L, Bollati-Fogolin M, Wickenhauser C, Krieg T, Muller W, Roers A. Interleukin-10 derived from macrophages and/or neutrophils regulates the inflammatory response to LPS but not the response to CpG DNA. *Eur J Immunol*. 2006;36(12):3248-3255.
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- **What opportunities for training and professional development has the project provided?**
 - *If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."*
 - *Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.*

This project has provided me with the opportunity to present my work as a Keynote Speaker for the National MD PhD student Annual Meeting in July 2018.

- **How were the results disseminated to communities of interest?**
 - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
 - *Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing*

public understanding and increasing interest in learning and careers in science, technology, and the humanities.

I have presented this work in oral format at grand rounds at Mayo Scottsdale and University of Washington, St. Louis.

- **What do you plan to do during the next reporting period to accomplish the goals?**
 - *If this is the final report, state "Nothing to Report."*
 - *Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.*

We will continue our current pace on experiments. We have submitted a manuscript of our current work to Blood and are currently awaiting reviews. We are also currently enrolling for a nutritional intervention in MPN with the purpose of determining whether a Mediterranean Diet can reduce inflammation in MPN.

4. Impact

Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

- **What was the impact on the development of the principal discipline(s) of the project?**
 - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
 - *Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

Our finding that persistent TLR signaling is seen in MPN and that this could potentially be a predisposing factor to acquire MPN has significant relevance for the development of preventative strategies in MPN. We are in the process of developing a protocol to investigate the impact of the anti-oxidant N-Acetylcysteine on protecting hematopoietic stem cells from the negative effects of chronic inflammation.

- **What was the impact on other disciplines?**
 - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
 - *Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.*

Nothing to Report

- **What was the impact on technology transfer?**
 - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
 - *Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*
 - *transfer of results to entities in government or industry;*
 - *instances where the research has led to the initiation of a start-up company; or*
 - *adoption of new practices.*

Nothing to Report

- **What was the impact on society beyond science and technology?**
 - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
 - *Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*
 - *improving public knowledge, attitudes, skills, and abilities;*
 - *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
 - *improving social, economic, civic, or environmental conditions.*

Our work has implications for prevention of hematologic malignancies via lifestyle interventions.

5. Changes/Problems

Nothing to Report

The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

- **Changes in approach and reasons for change**

No Changes

- *Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.*
- **Actual or anticipated problems or delays and actions or plans to resolve them**
 - *Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

None

- **Changes that had a significant impact on expenditures**

None

- *Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.*
- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

None

- *Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.*

6. Products

List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
Report only the major publication(s) resulting from the work under this award.
 - **Journal publications.** *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*
- Craver BM, El Alaoui K, Scherber RM, **Fleischman AG**. The Critical Role of Inflammation in the Pathogenesis and Progression of Myeloid Malignancies. *Cancers*, 2018 Apr 10(4) E104 PMID: 29614027
- Lee JS, Roberts A, Juarez D, Vo TT, Bhatt S, Herzog LO, Mallya S, Bellin RJ, Agarwal SK, Salem AH, Xu T, Jia J, Li L, Hanna JR, Davids MS, **Fleischman AG**, O'Brien S, Lam LT,

Levenson JD, Leta, A, Schatz JH, Fruman DA. Statins enhance efficacy of venetoclax in blood cancers. *Science Translational Medicine*, 2018 Jun 13;10(445): PMID: 29899021

- Singer JW, **Fleischman AG**, Al-Fayoumi S, Mascarenhas JO, Yu Q, Agarwal A. Inhibition of interleukin-1 receptor-associated kinase 1 (IRAK1) as a therapeutic strategy. *Oncotarget*, in press (accepted for publication Aug 15, 2018)
 - **Books or other non-periodical, one-time publications.** *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Fleischman AG and Van Etten RA. Pathogenesis of Myeloproliferative Neoplasm, Postgraduate Haematology, 7th Edition, 2018

- **Other publications, conference papers, and presentations.** *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Invited presentations at educational, governmental institutions (or similar organizations)

“Role of Inflammation in Myeloproliferative Neoplasm”, Mayo Arizona Hematology/Oncology Grand Rounds, Scottsdale, AZ, Sept 2017

“Myeloproliferative Neoplasm: Current Management and Future Directions, St. Vincent’s Hospital, Los Angeles, CA, Oct 2017

“Role of Inflammation in Myeloproliferative Neoplasm” Washington University Dept of Hematology Grand Rounds, St. Louis, MO, Nov 2017

Grand Rounds, Special Lectures

“Myeloproliferative Neoplasm”, MOASC Spotlight on Hematology, Huntington Beach, CA, Jan 2017

“Molecular Diagnostics in Chronic Myeloid Malignancies”, Second Annual Hematology Symposium, Anaheim, CA March 2017

“Myeloproliferative Neoplasm”, Leukemia Lymphoma Society Cancer Care Conference, Anaheim, CA, March 2017

“Role of Inflammation in Myeloproliferative Neoplasm”, We are MPN Conference, Irvine, CA April 2017

“Myeloproliferative Neoplasms and Clonal Hematopoiesis of Indeterminant Potential (CHIP): Implications for Health and Opportunity for Early Intervention/Prevention”, Clinica Romero, Los Angeles, CA, July 2017

“Shining a Light on MPNs”, Cancer Support Community-Benjamin Center, Los Angeles, CA Sept 2017

“Cancer Research”, American Cancer Society, Santa Ana, CA, Nov 2017

“Cancer Prevention and Research”, American Cancer Society Making Strides Against Breast Cancer Kickoff Event, Costa Mesa, Aug 2018

“Pathogenesis of Myeloproliferative Neoplasm”, Cancer Support Community-Benjamin Center, Los Angeles, CA Sept 2018

UCI Presentations:

“Role of Inflammation in Myeloproliferative Neoplasm”, Department of Medicine Research Retreat, Orange, CA, Dec 2016

“Role of Inflammation in Myeloproliferative Neoplasm”, Department of Medicine Research Retreat, Orange, CA, Dec 2017

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *biospecimen collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report

7. Participants & Other Collaborating Organizations

- **What individuals have worked on the project?**

- *Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."*

Example:

Name:	Mary Smith
Project Role:	Graduate Student

Researcher Identifier (e.g. ORCID ID):	1234567
Nearest person month worked:	5
Contribution to Project:	<i>Ms. Smith has performed work in the area of combined error-control and constrained coding.</i>
Funding Support:	<i>The Ford Foundation (Complete only if the funding support is provided from other than this award).</i>

Name:	Angela Fleischman
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-3701-6079
Nearest person month worked:	2
Contribution to Project:	Dr. Fleischman has designed the experiments, performed experiments, and analyzed data.
Funding Support:	DoD Career Dev Award, UC CRCC grant, Clinical Revenue, FTE from University of California

Name:	Daniel Kim
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	none
Nearest person month worked:	3
Contribution to Project:	Daniel has processed patient blood samples, performed in vitro assays, and analyzed data.
Funding Support:	DoD Career Development Award, V Foundation Scholar Award, Start Up package funds

Name:	Hew Yeng Lai
Project Role:	Graduate Student

Researcher Identifier (e.g. ORCID ID):	Does not have one
Nearest person month worked:	6
Contribution to Project:	Ms. Lai has processed patient blood samples, performed ELISA and intracellular staining experiments, and analyzed data.
Funding Support:	UC Irvine PhD program (covered by program not PI for first year of PhD)

Name:	Stefan Brooks
Project Role:	Graduate Student
Researcher Identifier (e.g. ORCID ID):	0000-0003-1670-1939
Nearest person month worked:	1
Contribution to Project:	Mr. Brooks has performed qPCR to assess SOCS3 expression.
Funding Support:	NCI T32 Training Grant

Name:	Brianna Craver
Project Role:	Graduate Student
Researcher Identifier (e.g. ORCID ID):	none
Nearest person month worked:	2
Contribution to Project:	Ms. Craver has performed ELISA to assess candidate compounds for their ability to reduce TNF.
Funding Support:	UC Irvine PhD program, Start Up Package

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
 - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*

- *If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

1/1/19-12/31/19 UC CRCC Grant, (\$75,000), “Effect of Diet in Myeloproliferative Neoplasm”
Role: PI

7/1/18-6/30/19 Chao Family Comprehensive Cancer Center Pilot Project Award (\$35,000)
“Dietary Intervention in Myeloproliferative Neoplasm”
Role: PI

10/1/17-9/30/19 MPN Research Foundation (\$20,000) “Dietary Intervention in Myeloproliferative Neoplasms”
Role: PI

- **What other organizations were involved as partners?**
 - *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
 - *Describe partner organizations - academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) - that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*

Nothing to report.

8. Special Reporting Requirements

- **COLLABORATIVE AWARDS:** *For collaborative awards, independent reports are required from **BOTH** the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.*
- **QUAD CHARTS:** *If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.*

Nothing to report.

9. Appendices

*Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc. Reminder: Pages shall be consecutively numbered throughout the report. **DO NOT RENUMBER PAGES IN THE APPENDICES.***

CV is included on the next pages.

CURRICULUM VITAE
ANGELA G. FLEISCHMAN M.D. Ph.D.
(other name used: Angela G. King)

Address: School of Medicine
839 Health Sciences Court
Sprague Hall, Suite 126
University of California, Irvine
Irvine, CA 92697

Telephone: 949-824-2559
Fax: 888-867-1020
E-Mail: agf@uci.edu

EDUCATION: Fellowship, Medical Oncology
Oregon Health & Science University
2007-2011

Residency, Internal Medicine
Oregon Health & Science University
2005-2007

Medical Doctor
Stanford University School of Medicine
2001-2005

Doctor of Philosophy, Cancer Biology
Stanford University School of Medicine
1998-2005

Bachelor of Science, Microbiology and Molecular Genetics
University of California, Los Angeles
1994-1997

ACADEMIC APPOINTMENTS:

2013 - Assistant Professor, School of Medicine, Department of Medicine Division of
Present Hematology/Oncology,
University of California, Irvine

2014 - Joint Faculty, School of Medicine, Department of Biological Chemistry
Present University of California, Irvine

2011 – Instructor, Department of Medicine, Division of Hematology & Medical Oncology
2013 Oregon Health & Science University

2011 – Staff Hematologist, Department of Medicine
2013 Portland Veterans Affairs Medical Center

NON-ACADEMIC APPOINTMENTS:

2014 - Leader, Hematologic Malignancies Disease Oriented Team, Chao Family Comprehensive
Present Cancer Center
University of California, Irvine

RESEARCH EXPERIENCE:

- 2013- University of California, Irvine
Principal Investigator of basic science laboratory
Research Focus: Pathogenesis of Myeloproliferative Neoplasm
- 2007-2013 Brian J. Druker Laboratory, Oregon Health & Science University
Medical Oncology Fellowship Research Focus: Pathogenesis of Myeloproliferative Neoplasm
- 1998-2005 Irving L. Weissman Laboratory, Stanford University School of Medicine
PhD Thesis: Molecular Mechanisms Involved in Commitment to the Lymphoid Lineage
- 1996-1998 Jeffrey H. Miller Laboratory, University of California, Los Angeles
Research Assistant: Archaeobacteria transcriptional regulation
Undergraduate Honors Thesis: Role of *E. Coli* DNA Pol ϵ in mutagenesis

LICENSES TO PRACTICE MEDICINE:

- 2013 - Present California
2011 - 2014 Oregon

BOARD CERTIFICATIONS:

- 2010 American Board of Internal Medicine, Internal Medicine
2013 American Board of Internal Medicine, Medical Oncology

MEMBERSHIPS IN PROFESSIONAL ORGANIZATIONS:

- 2009 – Present American Society of Hematology (ASH)
2010 – Present International Society for Hematology and Stem cells (ISEH)
2014 – Present Society of Hematologic Oncology (SOHO)
2014 – Present Medical Oncology Association of Southern California (MOASC)
2015 – Present University of California Hematologic Malignancies Consortium
2016 – Present South West Oncology Group (SWOG), Leukemia group
2017 – Present MPN Quality of Life Study Group

AWARDS AND HONORS:

- 2012 American Cancer Society Seed Research Grant
2014 Translational Research Training in Hematology Program
2014, 2017 MPN Challenge Award
2014 V Foundation Scholar Award
2018 Anti-Cancer Challenge Award

GRANTS, CONTRACTS AND RESEARCH AWARDS:**Current Grants**

- 1/1/19-12/31/19 UC CRCC Grant, (\$75,000), “Effect of Diet in Myeloproliferative Neoplasm”
Role: PI
- 7/1/18-6/30/19 Chao Family Comprehensive Cancer Center Pilot Project Award (\$35,000)
“Dietary Intervention in Myeloproliferative Neoplasm”
Role: PI
- 10/1/17-9/30/19 MPN Research Foundation (\$20,000) “Dietary Intervention in Myeloproliferative Neoplams”
Role: PI
- 10/1/17-9/30/19 MPN Research Foundation MPN Challenge Grant (\$200,000) “Inflammation as a

Driver of Clonal Evolution in MPN”
Role: PI

10/1/16-9/31/19 Department of Defense Career Development Award CA150493 (\$360,000)
“Inflammation as driver of clonal evolution in myeloproliferative neoplasm”
Role: PI

Pending Grants

9/1/18-8/31/20 NIH/NCI 1 R21 CA228099 (\$150,000 direct/year) “Preclinical Validation of Dual-
Modal Nanotherapy for Chronic Myeloid Neoplasms and Beyond”
Role: co-PI
Score: 5th percentile, awaiting payline

Past Grants

7/1/17-6/30/18 Committee on Research and Graduate Academic Programs 2016/2017 School of
Medicine/Pharmaceutical Science Faculty Research Grant (\$10,000) “Preclinical
Validation of Dual-Modal Nanotherapy for Chronic Myelogenous Leukemia and
Beyond”
Role: Co-PI

4/1/17-3/31/18 UC Irvine Institute for Clinical and Translational Science Pilot Grant (\$30,000)
“SMAC mimetics as a therapeutic approach in myeloproliferative neoplasm”
Role: PI

7/1/15-6/30/15 UC CRCC Grant (\$55,000) “Role of inflammation in Myeloproliferative Neoplasm”
Role: PI

1/1/15-12/31/15 Chao Family Comprehensive Cancer Center Seed Grant (\$100,000) “Advancing
Targeted Therapy for Hematologic Neoplasms”
Role: Co-PI

10/1/14-9/30/17 V Foundation for Cancer Research Scholar Award (\$300,000) “Pathogenesis of
calreticulin-mutated myeloproliferative neoplasm”
Role: PI

10/1/14 - 9/31/15 MPN Research Foundation/Leukemia Lymphoma Society MPN Challenge Grant
(\$100,000) “Role of Lymphocytes in the pathogenesis of myeloproliferative
neoplasm”
Role: PI

1/1/13 - 12/31/15 American Cancer Society Seed Grant, IRG – 98-279-07 (\$43,500) “Pathogenesis
of Myeloproliferative Neoplasm”
Role: PI

Faculty Mentored Awards

2018 Mentor. “Effect of Inflammation on Malignant Versus Wild-type Hematopoietic
Stem Cells.” 2018 School of Medicine Outstanding Student Fellowship. Brianna
Craver, Ph.D. candidate in Biological Chemistry.

2018 – 2019 Mentor. “Effect of Oxidative Stress on Mutant versus Wild-type Hematopoietic
Stem Cells.” T32 Post-doctoral Fellowship in Cancer Biology
PI: Gajalakshmi Ramanathan

2015 – 2017

Mentor. “Pathogenesis of Calreticulin Mutated Myeloproliferative Neoplasm”.
T32 Pre-doctoral Fellowship in Cancer Biology
PI: Stefan Brooks

PUBLICATIONS

Journal Articles-Peer Reviewed:

1. Slupska MM, **King AG**, Lu LI, Lin RH, Mao EF, Lackey CA, Chiang JH, Baikalov C, Miller JH. Examination of the role of DNA polymerase proofreading in the mutator effect of miscoding tRNAs. *J Bacteriol.* 1998; Vol 180(21),5712-7. PMID: 9791123
2. Kondo M, Scherer DC, Miyamoto T, **King AG**, Akashi K, Sugamura K, Weissman IL. Cell-fate conversion of lymphoid-committed progenitors by instructive actions of cytokines. *Nature* 2000; 407, 383-86. PMID: 11014194
3. Slupska MM, **King AG**, Fitz-Gibbon S, Besemer J, Borodovsky M, Miller JH. Leaderless transcripts of the crenarchael hyperthermophile *Pyrobaculum aerophilum*. *J Mol Bio.* 2001; Vol 309(2), 347-60. PMID: 11371158
4. Kondo M, Scherer DC, **King AG**, Manz MG, Weissman IL. Lymphocyte development from hematopoietic stem cells. *Current Opinions in Genetics and Development.* 2001; Vol 11(5), 520-26. PMID: 11532393
5. **King AG**, Kondo M, Scherer DC, Weissman IL. Lineage infidelity in myeloid cells with TCR gene rearrangement: A latent developmental potential of proT cells revealed by ectopic cytokine receptor signaling. *PNAS.* 2002; Vol 99(7), 4508-13. PMID: 11917122
6. Hsu C-L*, **King-Fleischman AG***, Lai AY, Matsumoto,Y, Weissman IL, Kondo M. Antagonistic action of C/EBP α and Pax5 in myeloid or lymphoid lineage choices in common lymphoid progenitors. *PNAS.* 2006; Vol 103, 672-677. *Authors contributed equally to this work
PMID: 16407117
7. Aichberger KJ, **Fleischman AG**, Deininger MW. Same mutation, different allele. *Blood.* 2009; Vol. 114(14), 3018-3023. PMID: 19797527
8. Bagby GC, **Fleischman AG**. The stem cell fitness landscape and pathways of molecular leukemogenesis. 2011; *Front Biosci (Schol Ed).* Vol 3:487-500. PMID: 21196392
9. **Fleischman AG**, Aichberger KJ, Luty SL, Bumm TG, Petersen CL, Dorototaj S, Vasudevan KB, LaTocha DH, Yang F, Press RD, Loriaux MM Pahl H, Silver RT, Druker BJ, Bagby GC, Deininger MW. Role of Tumor Necrosis Factor-alpha in clonal evolution of JAK V617F positive myeloproliferative neoplasm. *Blood.* 2011; Vol 118 (24):6392-6398. PMID: 21860020
10. **Fleischman, AG**. ALDH Marks Leukemic Stem Cells. *Blood.* 2012; Vol 119(15):3376-7. PMID: 22500050
11. **Fleischman AG**, Tyner JW. JAK2 V617F down-modulates MPL. *Blood.* 2012; Vol 119(20):4579-80. PMID: 22596167
12. **Fleischman AG***, Agarwal A*, Petersen CL*, Mackenzie R, Luty SL, Loriaux M, Druker BJ, Woltjer RL, Deininger MW. Effects of Plerixafor in combination with tyrosine kinase inhibition in a murine model of CML. *Blood.* 2012; Vol 120(13):2658-68. *authors have equal contribution. PMID: 22889761
13. **Fleischman AG**, Maziarz RT. Hematopoietic Stem Cell Transplantation for Myelofibrosis: Where Are We Now? *Current Opinion Hematology.* 2013; Vol. 20(2):130-6. PMID: 23314844

14. Sanda T, Tyner JW, Gutierrez A, Ngo VN, Glover JM, Chang BH, Yost A, Ma W, **Fleischman AG**, Zhou W, Yang Y, Kleppe M, Ahn Y, Tatarek J, Kelliher MA, Neuber DS, Levine RL, Moriggl R, Müller M, Gray NS, Jamieson CHM, Weng AP, Staudt LM, Druker BJ, Look AT. TYK2-STAT1-BCL2 Pathway Dependence in T-Cell Acute Lymphoblastic Leukemia. *Cancer Discovery*, 2013;Vol. 3(5):564-577. PMID: 23471820
15. Maxson JE, Gotlib J, Pollyea DA, **Fleischman AG**, Eide CA, Bottomly D, Wilmot B, McWeeney SK, Tognon CE, Pond JB, Collins RH, Deininger MW, Chang BH, Loriaux MM, Druker BJ, Tyner JW. Targetable CSF3R Mutations in Chronic Neutrophilic Leukemia and Atypical CML. *New England Journal of Medicine*, 2013; Vol. 368(19):1781-90. PMID: 23656643
16. **Fleischman AG**, Maxson JE, Luty SB, Agarwal A, Royer LR, Abel ML, Macmaniman JD, Loriaux MM, Druker BJ, Tyner JW. The CSF3R T618I mutation causes a lethal neutrophilic neoplasia in mice that is responsive to therapeutic JAK inhibition. *Blood*, 2013;122(22):3628-31. PMID: 24081659
17. **Fleischman AG**, Tyner JW. Causal role for JAK2^{V617F} in thrombosis. *Blood*, 2013; Vol.122(23):3705-6. PMID: 24288407
18. Agarwal A, Mackenzie RJ, Besson A, Jeng S, Carey A, LaTocha D, **Fleischman AG**, Duquesnes N, Eide CA, Vasudevan KB, Loriaux M, Firpo E, Cortes JE, McWeeney S, O'Hare T, Roberts JM, Druker BJ, Deininger MW*. BCR-ABL1 promotes leukemia by converting p27 into a cytoplasmic oncoprotein. *Blood*, 2014, Nov 20;124(22):3260-73. PMID: 25293778
19. Afrasiabi K, Zhou Y-H, **Fleischman AG**. Chronic inflammation: is it the driver or is it paving the road for malignant transformation? *Genes and Cancer*, 2015, May;6(5-6):214-9. PMID: 26124920
20. **Fleischman AG**. Inflammation as a Driver of Clonal Evolution in Myeloproliferative Neoplasm. *Mediators of Inflammation*, 2015:606819. doi: 10.1155/2015/606819. Epub 2015 Oct 11. PMID: 26538830
21. Brooks S, Luty SB, Lai HY, Morse SJ, Nguyen TK, Royer LR, Agarwal A, Druker BJ, **Fleischman AG**. JAK2^{V617I} results in cytokine hypersensitivity without causing an overt myeloproliferative disorder in a mouse transduction-transplantation model. *Experimental Hematology*, 2016 Jan Vol. 44(1):24-29 PMID: 26458983
22. Nguyen TK, Morse SJ, **Fleischman AG**. Transduction-Transplantation Mouse Model of Myeloproliferative Neoplasm. *Journal of Visualized Experiments. J Vis Exp*. 2016 Dec 22;(118). PMID: 28060252
23. Zhang J, **Fleischman AG**, Wodarz D, Komarova NL. Determining the role of inflammation in the selection of JAK2 mutant cells in myeloproliferative neoplasms. *J Theor Biol*, 2017 May 10;425:43-52. PMID: 28501635
24. Craver BM, El Alaoui K, Scherber RM, **Fleischman AG**. The Critical Role of Inflammation in the Pathogenesis and Progression of Myeloid Malignancies. *Cancers*, 2018 Apr 10(4) E104 PMID: 29614027
25. Lee JS, Roberts A, Juarez D, Vo TT, Bhatt S, Herzog LO, Mallya S, Bellin RJ, Agarwal SK, Salem AH, Xu T, Jia J, Li L, Hanna JR, Davids MS, **Fleischman AG**, O'Brien S, Lam LT, Levenson JD, Leta, A, Schatz JH, Fruman DA. Statins enhance efficacy of venetoclax in blood cancers. *Science Translational Medicine*, 2018 Jun 13;10(445): PMID: 29899021
26. Singer JW, **Fleischman AG**, Al-Fayoumi S, Mascarenhas JO, Yu Q, Agarwal A. Inhibition of interleukin-1 receptor-associated kinase 1 (IRAK1) as a therapeutic strategy. *Oncotarget*, in press (accepted for publication Aug 15, 2018)

Peer Reviewed Manuscripts Submitted:

1. Lai HY, Brooks S, Craver B, Morse SJ, Nguyen TK, Haghghi N, Luty SB, Garbati MR, **Fleischman AG**. Defective Negative Regulation of Toll-like Receptor Signaling Contributes to Excessive TNF- α Production in Myeloproliferative Neoplasm. *Blood*, (submitted Aug 24, 2018)

Peer Reviewed Manuscripts in Preparation:

1. Nguyen TK, Tata PV, Craver B, Brooks SA, Jena N, Morse SJ, Lai HW, Liu Z-Y, Rezk S, Oh ST, Van Etten RA, **Fleischman AG**. Critical but Distinct Roles for STAT5 and ERK in a Murine Model of Calreticulin Mutated Myeloproliferative Neoplasm. To be submitted to *Blood*
2. Brooks SA, Kim D, Morse SJ, Lai HY, Craver B, **Fleischman AG**. Upregulation of Endogenous Thrombopoietin Receptor MPL in CALR mutated Ba/F3 cells is selected during *in vivo* passage in mice demonstrating selectivity for MPL as chaperone for CALR. To be submitted to *Leukemia*
3. Craver B, Brooks SA, Lai SJ, Nguyen J, Nguyen H, **Fleischman AG**. SMAC mimetic LCL-161 selectively targets JAK2V617F mutant cells and reduces myelofibrosis and splenomegaly *in vivo*. To be submitted to *Clinical Cancer Research*

Book Chapters - Peer Reviewed

1. Fleischman AG and Van Etten RA. Pathogenesis of Myeloproliferative Neoplasm, Postgraduate Haematology, 7th Edition, 2018

Posters at Professional Conferences

1. **Fleischman AG**. Metastatic phyllodes tumor, American College of Physicians Oregon Chapter meeting, Nov 2005, Eugene, OR
2. **Fleischman AG**, Hsu, C-L, Lai, AY, Matsumoto Y, Weissman IL, and Kondo M. Antagonistic Effect of C/EBP α and Pax5. American Society of Hematology Annual Meeting, Dec 2005, Atlanta, GA
3. **Fleischman AG**, White K. A New Autoimmune Blistering Disease? American College of Physicians Oregon Chapter meeting, Dec 2006, Eugene, OR
4. Aichberger KJ, **Fleischman AG**, Doratotaj S, Bumm TG, Silver RT, Deloughery TG, Pahl HL, Druker BJ, Burns CJ, and Deininger MW. Tumor Necrosis Factor-Alpha (TNF) Expression Is Elevated in Myeloproliferative Neoplasms (MPN) and Modulated by Inhibition of JAK2 V617F. American Society of Hematology Annual Meeting, Dec 2009, New Orleans, LA
5. Agarwal A, **Fleischman AG**, Petersen CL, Loriaux MM, Woltjer R, Druker BJ, and Deininger MW. Effects of Plerixafor (AMD3100) In Combination with Tyrosine Kinase Inhibition In a Murine Model of CML. American Society of Hematology Annual Meeting, Dec 2011, Orlando, FL
6. **Fleischman AG**, Luty SB, LaTocha DH, Bagby GC, Druker BJ. Immune-mediated suppression of myelopoiesis in MPN. European School of Hematology Myeloproliferative Neoplasm International Conference, Oct 2012, Vienna, Austria
7. Sanda T, Tyner JW, Gutierrez A, Ngo VN, Glover JM, Chang BH, Yost AJ, Weng AP, Ma W, Tatarek J, **Fleischman AG**, Ahn Y, Yang Y, Zhou W, Neuberg DS, Moriggi R, Müller M, Kelliher M, Jamieson C, Gray NS, Staudt LM, Druker BJ and Look T. TYK2-STAT1 Pathway Positively

Regulates BCL2 Gene Expression in T-Cell Acute Lymphoblastic Leukemia. American Society of Hematology Annual Meeting, Dec 2012, Atlanta, GA

8. Maxson JE, Gotlib J, **Fleischman AG**, Eide CA, Bottomly D, Wilmot B, PhD, McWeeney S, Tognon C, Loriaux MM, Druker BJ and Tyner JW. A Truncation Mutant of CSF3R, Identified as a Novel Driver in De Novo Myeloid Leukemia, Signals through TNK2, and is Responsive to Dasatinib. American Society of Hematology Annual Meeting, Dec 2012, Atlanta, GA.
9. **Fleischman AG**, Luty SB, Garbati MR, Edmiston EB, LaTocha DH, Bagby GC and Druker BJ. Exaggerated response to Toll-like receptor agonist contributes to excessive TNF production in myeloproliferative neoplasm. International Society of Hematology and Stem Cells Annual Meeting, Aug 2013, Vienna, Austria
10. **Fleischman AG**, Luty SB, Garbati MR, Edmiston EB, LaTocha DH, Bagby GC and Druker BJ. Exaggerated response to Toll-like receptor agonist contributes to excessive TNF production in myeloproliferative neoplasm. American Society of Hematology Annual Meeting, Dec 2013, New Orleans, LA
11. Morse SJ, Luty SB, Lai HY, Druker BJ, **Fleischman AG**. T Mediated Suppression of Hematopoiesis in Myeloproliferative Neoplasm. American Society of Hematology Annual Meeting, Dec 2014, San Francisco, CA
12. Lai HY, Morse SJ, Luty SB, Garbati MR, Edmiston JB, Bagby GC, Druker BJ, Angela G **Fleischman AG**. Exaggerated Response to Toll-like Receptor Agonist Contributes to Excessive TNF Production in Myeloproliferative Neoplasm. American Society of Hematology Annual Meeting, Dec 2014, San Francisco, CA
13. Brooks S, Luty SB, Lai HY, Royer LR, Morse SJ, **Fleischman AG**. Expression of JAK2^{V617I} Does Not Result in Overt Myeloproliferative Disorder, but Results in Cytokine Hypersensitivity. American Society of Hematology Annual Meeting, Dec 2014, San Francisco, CA
14. Brooks S, Lai HY, Nguyen T, Morse S, **Fleischman AG**. Investigating the role of Calreticulin in Hematopoiesis. Cancer Biology Training Consortium Annual Meeting, Oct 2015, Kiawah Island, SC
15. Lai HY, Morse SJ, Nguyen TK, Luty SB, Garbati M, Bagby GC, Druker BJ, **Fleischman AG**. A Blunted Response to the Anti-Inflammatory Cytokine IL-10 Contributes to Excessive TNF Production in Myeloproliferative Neoplasm. American Society of Hematology Annual Meeting, Dec 2015, Orlando, FL
16. Kim TK, Huynh C, Zhao WM, Morse SJ, Lai HY, Brooks SA, **Fleischman AG**. SMAC mimetics as a therapeutic approach in myeloproliferative neoplasm. ICTS Translational Research Annual Meeting, June 2016, Irvine, CA
17. Brooks S, Lai HY, Nguyen TK, Morse S, **Fleischman A**. Investigating the role of Calreticulin in Hematopoiesis. Cancer Biology Training Consortium Annual Meeting. Oct 2016, Pittsburgh, PA
18. Lai HY., Morse S, Craver B, Brooks S, Nguyen, TK, FleischmanA. Defective IL-10 signaling contributes to the Chronic Inflammation in Myeloproliferative Neoplasm. La Jolla Immunology Conference, Oct 2017, San Diego, CA
19. Craver BM, Nguyen H, Lai HY, Kim D, Morse S, and **Fleischman AG**. JAK2V617F hematopoietic stem cells exhibit a blunted response to acute inflammation. Poster presentation, American Society of Hematology Conference, Dec 2017, Atlanta, GA.
20. Brooks SA, Morse SJ, Craver BM, Lai HY, Nguyen TK, Kim D, **Fleischman AG**, Tata P, Jena

N, Liu Z-Y, Van Etten RA. Overexpression of Calreticulin Impairs Self-Renewal Capacity of Hematopoietic Stem Cells. American Society of Hematology Conference, Dec 2017, Atlanta, GA.

21. Scherber RM, Morse SJ, Leproux A, Craver BM, Lai HY, Geyer H, Dueck AC, Palmer J, Padrnos L, Mesa RA, **Fleischman AG**. Needs and Preferences Regarding Nutrition and Supplement Use Among Individuals with Myeloproliferative Neoplasms: A Focus Group Study. American Society of Hematology Conference, Dec 2017, Atlanta, GA.
22. Scherber RM, Langlais BT, Geyer G, Dueck A, Kororiek H, Johnston C, Padrnos L, Palmer J, **Fleischman AG**, Mesa RA. Nutrition and Supplement Use Characteristics in the Myeloproliferative Neoplasms: Results from the Nutrient Survey. American Society of Hematology Conference, Dec 2017, Atlanta, GA.
23. Scherber RM, Langlais BT, Kosiorek HE, Dueck A, Geyer H, Senyak Z, McCallister A, Cotter M, VanHusen B, Palmer J, Padrnos L, Harrison C, **Fleischman AG**, Mesa RA. Psychostimulant Use Among Myeloproliferative Neoplasm Patients. American Society of Hematology Conference, Dec 2017, Atlanta, GA.
24. Craver BM, Hoang S, **Fleischman AG**. In vivo and ex vivo analysis of JAK2V617F hematopoietic stem cell response to inflammation. International Society of Experimental Society Annual Meeting, Aug 2018, Los Angeles, CA
25. El Alaoui, Weihe C, Oliver A, Craver BM, Kim D, Lai HY, Brooks S, Martiny J, Whiteson K, **Fleischman AG**. Investigating the Role of the Gut Microbiome in the Inflammatory State of Myeloproliferative Neoplasms. University of California Hematologic Malignancies Consortium Annual Meeting, Sept 2018, Irvine, CA.
26. Juarez D, Nguyen F, Diep G, Brem E, **Fleischman A**, Fruman D. Statins Enhance the Efficacy of BH3 Mimetics in Multiple Myeloma. University of California Hematologic Malignancies Consortium Annual Meeting, Sept 2018, Irvine, CA

CLINICAL RESEARCH PROTOCOLS:

Observational Trials as PI

1. HS#2014-1709 "Hematologic Malignancies Biorepository"
Status: Accrual Ongoing (255 participants accrued thus far)
2. HS#2014-9995 "Role of inflammation in the pathogenesis of myeloproliferative neoplasm"
Status: Accrual Ongoing (90 participants accrues thus far)
3. HS#2017-3209 "Evaluating the microbiome in myeloproliferative neoplasm"
Status: Fully accrued (60 participants), to amend to expand cohort and add additional experiments
4. HS# 2017-3445 "The NUTRIENT Trial (NUTRitional Intervention among myEloproliferative Neoplasms Trial" Focus Groups to Refine a Nutritional Intervention
Status: Complete (14 participants accrued)

Investigator Initiated Interventional Trials as PI

1. HS#2018-4521 The NUTRIENT Trial (NUTRitional Intervention among myEloproliferative Neoplasms): Feasibility Phase
Status: IRB approved 8/17/18 – Open to accrual shortly

Pharma Trials, Site PI

1. HS# 2015-2479, "UCI 15-67: A Phase 2, Open-label, Translational Biology Study of Momelotinib in Transfusion-Dependent Subjects with Primary Myelofibrosis (PMF) or Post-polycythemia Vera or Post-essential Thrombocythemia Myelofibrosis (Post-PV/ET MF).
Status: Closed (2018-4473 is extension phase of this study)
2. HS# 2017-3687, "UCI 17-31: An Open-Label Phase 2 Study of Itacitinib (INCB039110) in Combination With Low Dose Ruxolitinib or Itacitinib Alone Following Ruxolitinib in Subjects With Myelofibrosis
Status: Open for Accrual (one patient enrolled, this was first patient to enroll at any of the sites in the nation)
3. HS# 2018-4473 "UCI 18-17: Extended Access of Momelotinib for Subjects with Primary Myelofibrosis (PMF) or Post-polycythemia Vera or Post-essential Thrombocythemia Myelofibrosis (Post-PV/ET MF)"
Status: Open for Accrual

INVITED PRESENTATIONS:

Abstracts Selected for Oral Presentations at Professional Conferences

1. **King AG**, Kondo M, Scherer D, Weissman IL. Signaling through ectopic cytokine receptor reveals a latent myeloid differentiation potential of lymphoid progenitors. American Association of Immunologists Annual Meeting, Apr 2001, Orlando, FL
2. **Fleischman AG**, Petersen CL, Aichberger KJ, LaTocha DH, Vasudevan KB, Druker BJ, Bagby GC, and Deininger MW. JAK2V617F induced TNF resistance as a mechanism of clonal expansion in Myeloproliferative Neoplasm. European School of Hematology Myeloproliferative Neoplasm International Conference, Oct 2010, Albufeira, Portugal
3. **Fleischman AG**, Aichberger KJ, Petersen CL, Doratotaj S, Bumm TG, Pahl HL, Druker BJ, and Deininger MW. Jak2 V617F Induced TNF Resistance as a Mechanism of Clonal Expansion In Myeloproliferative Neoplasm. American Society of Hematology Annual Meeting, Dec 2010, Orlando, FL
4. **Fleischman AG**, Sanda T, Gutierrez A, Luty SB, Willis SG, Look AT, Druker BJ, and Tyner JW. Mutationally Activated TYK2 From T-ALL Specimens Exhibits Transformative Capacity in Cell Lines and Primary Cell Models and T-Lineage Expansion in Mice. American Society of Hematology Annual Meeting, Dec 2011, San Diego, CA
5. **Fleischman AG**. The Fitness Landscape of the Hematopoietic Stem Cell Pool as a Driver of Neoplastic Clonal Evolution. Chao Family Comprehensive Cancer Center Annual Retreat, Nov 2013, Palm Springs, CA
6. Maxson JE, **Fleischman AG**, Luty SB, Royer LR, Agarwal A, Loriaux MM, Druker BJ, Tyner JW. CSF3R T618I Mouse Bone Marrow Transplant Model of Neutrophilic Leukemia. American Society of Hematology Annual Meeting, Dec 2013, New Orleans, LA
7. Maxson JE, Gotlib J, Pollyea D, **Fleischman AG**, Agarwal A, Luty SB, Abel M, Eide CA, Bottomly D, Wilmot B, McWeeney SK, Tognon CE, Pond JB, Collins RH, Goueli B, Oh ST, Deininger MW, Chang BH, Loriaux MM, Druker BJ, Tyner JH. The CSF3R T618I mutation found in Chronic Neutrophilic Leukemia removes an O-linked glycosylation site and increases receptor

dimerization. American Society of Hematology Annual Meeting, Dec 2013, New Orleans, LA

8. Nguyen TK, Tata PV, Brooks SA, Jena N, Morse SJ, Lai HY, Liu Z-Y, Van Etten RA, **Fleischman AG**. The MEK/ERK Inhibitor Trametinib Reduces Fibrosis in a Transduction-Transplantation Model of Mutated Calreticulin. 7th International Conference on Myeloproliferative Neoplasm, Oct 2016, Estoril, Portugal
9. Nguyen TK, Tata PV, Brooks SA, Jena N, Morse SJ, Lai HY, Liu Z-Y, Van Etten RA, **Fleischman AG**. The MEK/ERK Inhibitor Trametinib Reduces Fibrosis in a Transduction-Transplantation Model of Mutated Calreticulin. American Society of Hematology Annual Meeting, Dec 2016, San Diego, CA
10. Scherber RM, Langlais BT, Geyer HL, Dueck A, Johnston C, Kosoriek H, Padrnos L, Palmer J, Mesa RA, **Fleischman AG**. Nutrition and Supplement Use In The Myeloproliferative Neoplasms: Results from the NUTRIENT Survey. University of California Hematologic Malignancies Consortium Annual Meeting, Sept 2017, San Francisco, CA

Invited Presentations at National and International Conferences

1. "Excessive TNF production as a driver of clonal evolution in myeloproliferative neoplasm", La Jolla Immunology Conference, San Diego, CA Oct 2016
2. Keynote Speaker: "Inflammation as a Driver of Clonal Evolution in MPN", National MD/PhD Student Conference, Keystone, CO, July 2018

Invited Grand Rounds

1. "Inflammation in MPN" USC Hematology Grand Rounds, Los Angeles, CA, Oct 2015
2. "Myeloproliferative Neoplasm: Current Management and Future Directions, St. Vincent's Hospital, Los Angeles, CA, Oct 2017
3. "Role of Inflammation in Myeloproliferative Neoplasm", Mayo Arizona Hematology/Oncology Grand Rounds, Scottsdale, AZ, Sept 2017
4. "Role of Inflammation in Myeloproliferative Neoplasm" Washington University Dept of Hematology Grand Rounds, St. Louis, MO, Nov 2017
5. "Pathogenesis of Myeloproliferative Neoplasm" University of California San Francisco Hematologic Malignancies Section, San Francisco, CA, Nov 2018

Regional and Extramural Local Presentations

1. "Myeloproliferative Neoplasm", Gilda's Club, Palm Desert, CA, Sept 2015
2. "Myeloproliferative Neoplasm", Cancer Support Community, Los Angeles, CA, Sept 2015
3. "Myeloproliferative Neoplasm", MOASC Spotlight on ASH, Newport Beach, CA, Jan 2016
4. "Myeloproliferative Neoplasm", Leukemia Lymphoma Society Cancer Care Conference, Anaheim, CA, March 2016
5. "Myeloproliferative Neoplasm Nurses Education Program", Leukemia Lymphoma Society, Santa Barbara, CA, May 2016
6. "The MEK/ERK Inhibitor Trametinib Reduces Fibrosis in a Transduction-Transplantation Model of

Mutated Calreticulin”, University of California Hematologic Malignancies Consortium Research Symposium, San Diego, CA, Sept 2016

7. “Myeloproliferative Neoplasm Patient Education Seminar”, Cancer Support Community-Benjamin Center, Los Angeles, CA Sept 2016
8. “Myeloproliferative Neoplasm”, MOASC Spotlight on Hematology, Huntington Beach, CA, Jan 2017
9. “Molecular Diagnostics in Chronic Myeloid Malignancies”, Second Annual Hematology Symposium, Anaheim, CA March 2017
10. “Myeloproliferative Neoplasm”, Leukemia Lymphoma Society Cancer Care Conference, Anaheim, CA, March 2017
11. “Role of Inflammation in Myeloproliferative Neoplasm”, We are MPN Conference, Irvine, CA April 2017
12. “Myeloproliferative Neoplasms and Clonal Hematopoiesis of Indeterminant Potential (CHIP): Implications for Health and Opportunity for Early Intervention/Prevention”, Clinica Romero, Los Angeles, CA, July 2017
13. “Shining a Light on MPNs”, Cancer Support Community-Benjamin Center, Los Angeles, CA Sept 2017
14. “Cancer Research”, American Cancer Society, Santa Ana, CA, Nov, 2017
15. “Cancer Prevention and Research”, American Cancer Society Making Strides Against Breast Cancer Kickoff Event, Costa Mesa, Aug 2018

UCI Presentations

1. “Inflammation as a driver of clonal evolution in Myeloproliferative Neoplasm”, UC Irvine Epidemiology Seminar Series, Irvine, CA, Feb 2014
2. “Inflammation as a driver of clonal evolution in Myeloproliferative Neoplasm”, UC Irvine Department of Biological Chemistry, Irvine, CA, March 2014
3. “Pathogenesis of Myeloproliferative Neoplasm”, UC Irvine Campuswide Symposium on Basic Cancer Research, Irvine, CA, May 2014
4. “Inflammation as a driver of clonal evolution in Myeloproliferative Neoplasm”, Stem Cell Awareness Day, Irvine, CA, Oct 2014
5. “The Physician Scientist”, UC Irvine Medical Interest Group, Irvine, CA, Nov 2015
6. “Role of Inflammation in Myeloproliferative Neoplasm”, Department of Medicine Research Retreat, Orange, CA, Dec 2016
7. “Role of Inflammation in Myeloproliferative Neoplasm”, Department of Medicine Research Retreat, Orange, CA, Dec 2017

Webinars

1. MPNs-state of the art in 2017 and beyond, *VuMedi*, Oct 2017
<https://www.vumedi.com/video/myeloproliferative-neoplasmsmpns-state-of-the-art-in-2017-and->

[beyond/?list=13f40c57-facd-438c-a47c-79035c309809](#)

2. Myeloproliferative Neoplasms (MPNs): Post-ASH 2017 Wrap Up and Future Directions, *VuMedi*, Feb 2018. <https://www.vumedi.com/video/intro-to-mpns-with-focus-on-myelofibrosis-prognostic-scoring-systems-old-and-new-from-ash-2017/?list=92951279-eb61-4e10-a553-519cd583e148>
3. What the experts learned at ASH, *Patient Power*, Dec 2017. <https://www.patientpower.info/video/the-latest-mpn-news-what-the-experts-learned-at-ash>

Radio and Media Interviews

1. Polycythemia Vera, *Frankly Speaking About Cancer Radio Show*, Dec 2015
2. Cancer Research, *KFROG FM*, Aug 2017
3. Role of Inflammation in MPN, PV Reporter Video Interview, Dec. 2018 <http://www.pvreporter.com/dr-angela-fleischman-shares-the-latest-research-on-inflammation-in-mpns-at-ash-2015/>.

UNIVERSITY SERVICE

2014 - Present	Leader, Hematologic Malignancies Disease Oriented Team
2014 - Present	Member, Radiation Safety Committee, Dept of Medicine representative
2015 - Present	Member, human stem cell research oversight (hSCRO) Committee
2016 - Present	Departmental Representative, COHS Representative Assembly
2016 - Present	Cancer Research Institute High School Summer Program Mentor
2017, 2018	Excellence in Research Oral Presentation Mediator
2017	Reviewer, ACS Seed Grants, Chao Family Comprehensive Cancer Center
2017	Reviewer, Chao Family Comprehensive Cancer Center Pilot Grant
2017, 2018	Reviewer, ICTS Translational Science Pilot Grant
2017- 2018	Mentor, Medical Student Research Program
2018	BioSci-SOM Pilot Funding for Faculty Pursuing Collaborative Research
2018	Reviewer, Faculty Mentor Program Fellowship
2018	Reviewer, President's Dissertation Year Fellowship

SERVICE TO PROFESSIONAL SOCIETIES & COMMITTEES

2015	Abstract Reviewer, American Society of Hematology
2016	Abstract Reviewer, European Hematology Association
2018	Abstract Reviewer, University of California Hematologic Malignancies

Consortium
2018 Chair, University of California Hematologic Malignancies Annual Conference

EDITORIAL BOARD SERVICE

2018-present [HemeOnc Times](#)

SERVICE AS REVIEWER OF MANUSCRIPTS AND REFEREE OF EXTRAMURAL PROPOSALS

Journals:
2013-present [Blood](#)
[Leukemia](#)
[Haematologica](#)
[Oncogene](#)
[Oncotarget](#)
[Cancer](#)
[PlosOne](#)

Leukemia Lymphoma Society
2016 Transforming CURES Grant Reviewer

COMMUNITY SERVICE

2014-2017 Leukemia Lymphoma Society Man/Woman of the Year Campaign Committee
Attended monthly meetings to organize campaign and hosted lab tour events

2004-2017 Leukemia Lymphoma Society Cancer Care Conference Steering Committee
Selected speakers and recruited them to speak

2015 – Present Founder, We are MPN
Educational Foundation and website that provides resources for MPN patients for research, clinical trials, and educational events. Over 1500 website visits since its creation

2018 – Present Founder, Orange County MPN Education Group
Over 50 MPN patients and supporters meet quarterly for educational activities focused on MPN

CONFERENCE CHAIR

Oct 2015 We are MPN Patient Education Conference, Irvine, CA

Apr 2017 We are MPN Patient Education Conference, Irvine, CA

Jan 2018 Medical Oncology Society of Southern California Spotlight on Hematology, Huntington Beach, CA

Sept 2018 University of California Hematologic Malignancies Consortium Annual Meeting, Irvine, CA

TEACHING AND MENTORING

Teaching

2014	Mol Biol 217B Cancer Biology <i>Led 1 lecture and 2 journal club sessions</i>
2016	BIO SCI 25 Biology of Cancer <i>One hour lecture on cancer fundamentals and leukemia, introductory undergraduate class</i>
2017	BIO SCI 25 Biology of Cancer <i>One hour lecture on cancer fundamentals and leukemia, introductory undergraduate class</i>
2018	MBB 221 Advanced Topics in Immunology: Concepts and Literature <i>Led two classes involving selection and discussion of articles, creation of final exam and grading of final exam</i>
2018	Cancer Biology Journal Club for T32 trainees, Leader <i>Work with students to select journal articles to discuss and mediate discussion, 2 hours per week x 10 weeks</i>

Mentoring

Undergraduates

2013 – 2014	Hew Yeng (Betty) Lai, Project: Mechanism of excessive TNF production in MPN
2014 – 2015	Deepicka Mehta, Project: IFN α signaling in MPN
2015 – 2016	William Zhao, Project: therapeutic sensitization of JAK2V617F cells to TNF
2015 – 2016	Azadeh Fatehi Shalamzari, Project: role of calreticulin in hematopoiesis
2016 – 2018	Jenny Nguyen, Project: role of inflammation in MPN Excellence in Research Designation
2016 – 2018	Hellen Nguyen, Project: SMAC mimetics as a therapeutic approach to MPN Excellence in Research Designation
2017 – Present	Harleen Mehrok, Project: Pathogenesis of Calreticulin Mutated MPN
2017 – Present	Summer Hoang, Project: modeling Calreticulin mutated MPN
2017 – Present	Ella Chang, Project: Mechanism of excessive TNF production in MPN
2018 – Present	Tiffany Trieu, Project: N-AC as a therapy in MPN
2018 – Present	Tiffany Han, Project: TBD

PhD Rotation Students

2014	Melanie Studzinski
2014	Tuyen Nguyen
2015	Jessica Flescher

2015 Ziguang (Bob) Lin
2015 Member of Academic Hearing Panel
2015 Quy Nguyen
2017 Anastasia Ionkina
2017 James Titorjhardo

PhD Thesis Students

2014 – Present Stefan Brooks, Project: Pathogenesis of Calreticulin Mutated MPN
2016 – Present Brianna Craver M.S., Project: Differential Effects of Inflammation on Malignant versus Normal Hematopoietic Stem Cells
2016 – Present Hew Yeng (Betty) Lai, Project: Mechanism of Persistent TNF Production in MPN
2018 – Present Laura Mendez M.D., Project: Effect of Diet on the Pathogenesis of Myeloproliferative Neoplasm

Post-doctoral fellows

2015 – 2017 Thanh Kim Nguyen, Ph.D., Project: Role of T cells in Myeloproliferative Neoplasm
Current position: Staff Scientist at Kite Pharma, Santa Monica, CA
2018 – Present Gajalakshmi Ramanathan Ph.D., Project: Effect of smoking on disease pathogenesis of myeloproliferative neoplasm.

Clinical fellows

2018 – Present Carolyn Haunschild M.D., Gynecologic Oncology Fellow. Project: Investigating the Microbiome in the Gynecologic Cancers

Visiting Scholars

2018 – Present Kenza El Alaoui M.D., Internal Medicine Resident from Belgium. Project: Investigating the Microbiome in MPN