Approach Template: R01

1-2 sentences “Specific Aim 1: To ...” List your first Specific Aim. This is a major heading so Bold it. Copy exactly from the Specific Aims page.

1-2 paragraphs Begin by reiterating the premise behind this specific aim (Rationale). Briefly remind your reviewers what you are studying, reiterate your hypothesis, the significance, and what you hope to achieve.

1-2 paragraphs Briefly describe any background necessary to understand the context of the Specific Aim. Explain what was previously known and what the deficit in knowledge is.

1 page Present your published data to support your hypothesis and/or the feasibility of the studies. If there are any key figures necessary to understand the work or to establish feasibility, reproduce them here. Provide everything the reviewers will need to understand and appraise your application. Make sure Reviewers can distinguish your data from others.

1-2 pages Present any additional unpublished preliminary data to support the feasibility of your Specific Aim and to show you can interpret results. Don’t waste space BUT make sure figures are neat and big enough to be read easily. Additional preliminary data can be placed wherever needed to support aims or specific experiments.

4-5 sentences Provide an overview of the sets of experiments to be performed explaining what you are testing and what methodologies will be employed. IT IS CRITICAL THAT THESE EXPERIMENTS CAN TEST YOUR HYPOTHESIS OR HYPOTHESES.

1/2 – 1 Page Explain the methodological approach. Provide references to methods or reference preliminary data (e.g. Fig. X) to establish feasibility of non-standard or complex techniques.

1/2 – 1 Page If relevant provide details on animal models (sex, age, drug regimes, and doses, mouse strains, KO or transgenic mice and what their appropriate WT controls are and what makes them ideal for your studies). If relevant provide details of human populations including, demographic data, sex selection, age selection, disease state, normal or other controls. Provide Inclusion and exclusion criteria. Use flow or other diagrams to clarify complex experimental designs and to delineate experimental arms.

1-2 paragraphs Interpret your data: Expected outcomes. Explain what your expected outcome is for each experiment listed and how you will recognize that outcome based on the methods used. Explain what this outcome will mean in terms of your
hypothesis and the significance of this outcome to the big picture (moving the field forwards and for human health).

<1 paragraph> **Interpret your data: Alternative Outcomes.** Experiments don’t always provide the expected data. Show that you have thought through the possible outcomes and explain what will be concluded if the outcome is different than expected. Focus on the positive. Will you learn something important even if the data is not as anticipated? Will you be able to devise a different hypothesis? How might you test it?

<1 paragraph> **Caveats and alternative approaches:** Are there any constraints, limitations of models, patient populations, or in the methodology that could preclude a definitive answer or lead to a failed experiment? Try to think of a solution and pose an alternative strategy for major caveats. Don’t list more than one or two major caveats, or a reviewer may doubt the feasibility of the approach. In an ideal world preliminary data will have already established feasibility and will mitigate the potential for unanticipated outcomes and technical failures.

<1 paragraph> **Provide Power Analysis** for animal group size and/or human subjects. Justify the feasibility of achieving these numbers in the proposed time frame (especially for human subject recruitment).

<5-10 lines> **Provide a clear description of the Statistical Analysis to be employed.** Remember to consider both parametric and non-parametric tests and to explain how you will assess which is appropriate to use. Explain how you will perform simple comparisons, group comparisons, paired or unpaired data, etc. based on the studies you are proposing. State clearly what you will consider significant (e.g. P < or = 0.05). If you plan on using a statistical service or have a dedicated statistician working on the project provide less detail on the statistics BUT provide and refer to a letter of support/collaboration documenting their role.

<3-4 sentences> **Outline and justify your Time Line** for the studies in the Specific Aim (Years X to Y). If necessary explain any expected delays (mouse breeding or aging, patient recruitment etc) and when you expect to complete the aims. This can be optionally placed at the end of the Specific Aims to cover all Aims. Use a diagram if necessary.

< As Above> **Repeat the steps above for additional Specific Aims.** Do not unnecessarily duplicate information (e.g. preliminary figures, animal models, methods etc.) from Previous Aims, simply refer the Reader back, but be specific as to where the information is located. Using numbered sections can be helpful if there is a lot of back referencing. For a new investigator 2 strong Specific Aims is usually sufficient.