Peer Review File

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Major Comments:
The authors have assembled an extremely ambitious review of the extensive (and confusing!) literature on ATF3 in atherosclerosis, and should be commended for doing so. On the whole, the review is well organized and well written (with the exception of an extensive list of English as a second language grammatical oddities noted with suggested changes below).
Ironically, the exhaustive depth of the review somewhat harms its overall quality: papers are mostly distilled to one or two sentences, and discrepant findings between tissues or studies are simply reported, rather than discussed critically. The addition of some figures would considerably increase the accessibility and usefulness of this review for readers. Specifically a summary of the splice isoforms, different promoters, and the upstream regulators that influence them would have been helpful. Similarly, a graphical representation of the tissue/cellular contexts of the major pathways/gene sets downstream of ATF3 would be a nice addition.

Minor Comments/corrections:
line 49 r/contain/include/
line 62 r/regulator of cellular/regulator of the cellular/
line 128 weird sentence: Besides, ATF3Δzip was also reported to be correlated with human hypospadias (suggest deleting, this has nothing to do with the main subject matter or theme of the journal)
line 139 r/in gliomal cell/in gliomal cells
line 199 r/shown no/showed no
line 213ff:
He et al. certified that early growth response gene 1 (Egr-1) mediates ATF3 overexpression by stabilizing ATF3 mRNA in glomerular mesangial cells(GMCs) upon sublytic C5b-9 stimulation, while the binding site remains unclear
While the binding site remains unclear, He et al. demonstrated that early growth response gene 1 (Egr-1) mediates ATF3 overexpression by stabilizing ATF3 mRNA in glomerular mesangial cells(GMCs) upon sublytic C5b-9 stimulation.
line 238 r/Latter/Later
line 240 r/On the contrary/In contrast
line 268 r/support that/supports the notion that
line 277 TRLs is more commonly used (instead of TGRLs)
line 285 r/Besides/In another study,
line 295 r/disclosed that ATF3 mediated a protective effect by attenuating/described an ATF3-mediated protective effect in attenuating
line 296 r/through a/through an
line 347 r/Besides, VSMC is another major source of foam cell in atherosclerosis/[delete 'Besides,']VSMCs are another major source of foam cells in atherosclerosis
line 349 r/supported that/supports the notion that

line 367 r/through the genome-wide/through genome-wide
line 377 I'm unclear what the authors' intended meaning is by "Although the nullity of hypoglycemic therapy in vascular complications of diabetic mellitus (DM) has been well proven"
Do they mean that 'hypoglycemic therapy has proven to be ineffective in limiting vascular complications that result from T2DM'?
line 380 r/diversified/varied
line 472 r/has been gradually perceived for decades/has gradually emerged over the past two decades
line 482 r/should attach more attention to further research/suggest that more attention is merited
line 483 r/worthy of trace and summary/worthy of deeper investigation
line 487 r/advance/advances
line 488 r/makes/make (to agree in number with the 'advances' change in the preceding line
^it's not clear what specific molecular-targeted therapy the authors have in mind. This should be accompanied with a citation
line 490 r/furtherly put forward/advance

This was NOT an easy ready - very, very dry and dense. I strongly suggest that the addition of some figures would increase its usefulness.

Response: Thanks for your valuable comments and careful revision, we've corrected the improper expression followed your corrective comments and some suggestions from the professional medical editing service. We've also added the needful figures to summarize the regulatory mechanism and specific role of ATF3 in atherosclerosis, as well as the transcript variants of ATF3.

Actually, we found that the regulatory mechanism of ATF3 reported in different studies is extremely complex, even contradictory. The regulatory diversity of ATF3 compelled us to draw a comprehensive description and waive the profound discussion due to limited length.

Thank you again for your affirmation of this work.

Change in the text: we have added some figures to increase the usefulness of this work. (See Page 11, Line 177; Page 14, Line 211; Page 23, Line 368; Page 30, Line 493). And we have also modified our text as advised.
(See:
Page 4, Line 74 r/include
Page 5, Line 88 r/regulator of the cellular
Page 11, Line 176 weird sentence have been deleted as advised
Page 12, Line 193 r/ glioma cells
Page 18, Line 279 r/ did not differ
Page 19, Line 296 r/ While the binding site remains unclear, He et al. demonstrated that early growth response gene 1 (Egr-1) mediates ATF3 overexpression by stabilizing ATF3 mRNA in glomerular mesangial cells (GMCs) upon sublytic C5b-9 stimulation.
Page 20, Line 327 r/ Later
Page 21, Line 330 r/ conversely
Page 23, Line 365 r/ supports the notion that

Page 23, Line 385 r/ TRLs
Page 24, Line 395 r/ In another study,
Page 25, Line 406 r/ described an ATF3-mediated protective effect in attenuating
Page 25, Line 407 r/ through an
Page 28 Line 463 r/ Another major source of foam cells in atherosclerosis AS is VSMC
Page 28 Line 465 r/ supports the notion that
Page 29 Line 489 r/ genome-wide
Page 31 Line 510 r/ Hypoglycemic therapy has proven to be ineffective in limiting vascular complications that result from T2DM
Page 31 Line 514 r/ varied
Page 38 Line 625 r/ has gradually emerged over the past two decades
Page 38 Line 637 r/ suggest that more attention is merited
Page 38 Line 638 r/ worthy of deeper investigation
Page 38 Line 642 r/ advances. (a citation have been added)
Page 38 Line 646 r/ advance.)