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Viewpoint

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# Novel Quinolinones as Activators of AMP Activated Protein Kinase

## Patent Highlight

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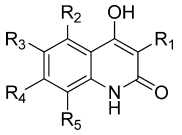
| **Title:** | Novel Quinolinones as Activators of AMP Activated Protein Kinase | | |
| **Patent/Patent Application Number:** | WO 2012119978A1 | **Publication date:** | September 13, 2012 |
| **Priority Application:** | US 2011-449853P | **Priority date:** | March, 7, 2011 |
| **Inventors:** | Daugan, A. C.-M.; Lamotte, Y.; Mirguet, O. | | |
| **Assignee Company:** | Glaxo-Smithkline, LLC | | |
| **Disease Area:** | Neurodegenerative diseases, diabetes, mitochondrial disorders | **Biological Target:** | AMPK |

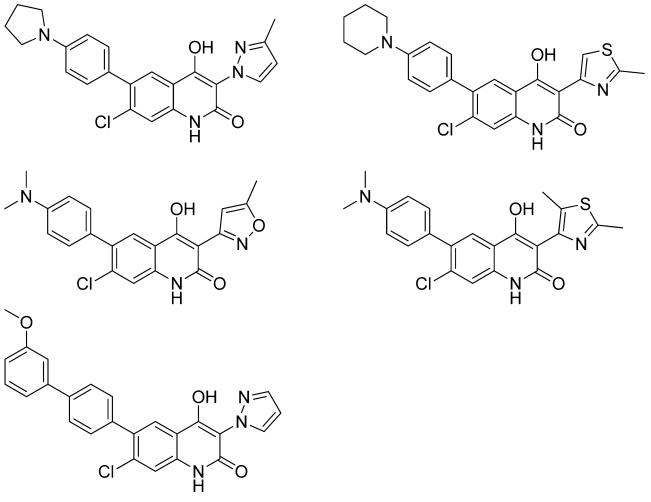
**Summary:**

This application claims a series of quinolinones, which are activators of AMP activated protein kinase (AMPK), as potential treatment for various diseases mediated by AMPK. The involvement of AMPK in the regulation of cellular and whole body energy metabolism has become apparent, and activators of AMPK could have beneficial effect in preventing diseases, such as heart disease, metabolic syndrome, and neurodegenerative diseases, e.g. Alzheimer's disease.

**Important Compound Classes:**




**Key Structures:**




**Recent Review Articles:**

1. Verdaguer, E.; Junyent, F.; Folch, J.; Beas-Zarate, C.; Auladell, C.; Pallas, M.; Camins, A. Aging biology: a new frontier for drug discovery. *Expert Opin. Drug Discovery* 2012, *7* (3), 217−229.

2. Amato, S.; Man, H.-Y. Bioenergy sensing in the brain. The role of AMP-activated protein kinase in neuronal metabolism, development and neurological diseases. *Cell Cycle* **2011**, *10* (20), 3452−60.

3. Kodiha, M.; Stochaj, U. AMP kinase: the missing link between type 2 diabetes and neurodegenerative diseases? *Trends Mol. Med.* **2011**, *17* (11), 613−614.

**Biological Assay:** Human recombinant AMPK was used in a FRET assay.

**Biological Data:** One hundred and ninety-six compounds were tested. The five structures described above were evaluated in an AMPK enzymatic assay and had an average $pEC_{50}$ < 5.5 and $pEC_{200}$ values less than 5.

**Special Issue:** Alzheimer's Disease

**Published:** October 24, 2012

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| **Synthesis:** | Preparation of 196 compounds. |
| **Claims:** | Claim 11: Use of quinolinones for the manufacture of a medicament for treating a variety of diseases, including diabetes, metabolic syndrome, atherosclerosis, mitochondrial disorders, schizophrenia, neuroinflammation, multiple sclerosis, ALS, and Alzheimer's disease. |

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### Notes

The authors declare no competing financial interest.