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This issue of Il Nuovo Cimento is dedicated to the workshop Quantum Gravity, Higher Derivatives and Nonlocality (QGRAV 2021). The aim of the workshop was to assess our current understanding of the interplay between gravity and quantum mechanics, with particular attention to what the main role of higher derivatives and nonlocality is in the formulation of a consistent theory of quantum gravity, and whether they are really necessary to describe Nature at a fundamental level. The workshop has triggered new insights about fundamental physics and our understanding of the Universe through focused and constructive debates.