The goal of this paper is twofold: first, we aim to assess the role played by inventors’ cross-regional mobility and collaborations in fostering knowledge diffusion across regions and subsequent innovation. Second, we intend to evaluate the feasibility of using mobility and co-patenting information to build cross-regional interaction matrices to be used within the spatial econometrics toolbox. The present inquiry is a first step in this direction and estimates a knowledge production function (KPF) where geographical interactions occurring across regions in the production of knowledge are introduced. Specifically, a more meaningful modelling of these interactions through inventors’ mobility and co-patenting data has been considered when building weights matrices to describe the strength of bilateral knowledge relations across European regions.