Amidst the Vatican collections containing material in Greek, there are a number of manuscripts that were most definitely produced in the environment of the Patriarchate of Constantinople during various periods. The importance of these witnesses lies in the fact that they often surprisingly come from Byzantine contexts most hostile to the rapprochement with the Church of Rome. The channels through which these manuscripts arrived in Rome are most diverse, and often the conclusion of the course is completely unexpected, at least if the perspective of those who produced them is considered. The witnesses today in the Vatican Library linked to the context of the “Great Church” of Constantinople cover a good part of the Byzantine Millennium and later. I will focus on the late Byzantine period, especially on the second half of the thirteenth century, when, after the Fourth Crusade (1204 to 1261), the emperors of the Palaeologan dynasty attempted a work of reconstruction according to an assumed programmatic restoration of the imperial dignity and a revival of patriarchal jurisdiction over churches and monasteries. Moreover, we shall follow the work of copying literary and documentary texts within the patriarchal milieu through manuscripts related to figures showing their concrete interests in the theological disputes of the time as well as their direct involvement in the activities of the chancery office of the Orthodox primate until the first half of the fifteenth century - on the eve of the fall of Constantinople.