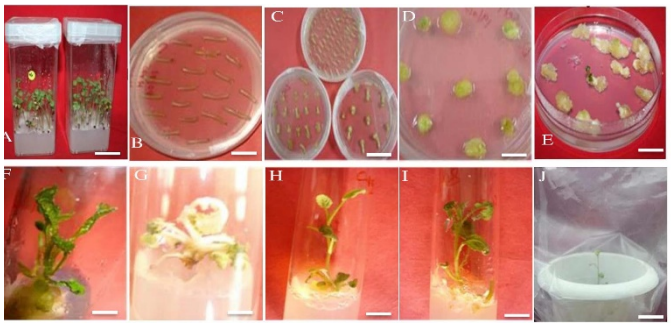**Figure S1**